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THE STORY OF THE GLOSSOPHARYNGEAL NERVE

AND FOUR CENTURIES OF RESEARCH CONCERNING THE CRANIAL NERVES OF MAN

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To a kindly and imaginative mind, somewhat imbued with neural anatomy, the glossopharyngeal nerve makes a sympathetic appeal. It stands alone among the twelve cranial apostles, as a nerve without any very definite or important physiology and without any disease attached to its functions. It has no tic or palsy, or algia; it shares with the fifth and tenth nerves in supplying touch, taste and deglutition. But it is not vital to these functions. It could be resected with impunity. It receives only disregard and aloofness from surgeon and clinician.

One hundred years ago, however, an author brought to the ninth cranial nerve a certain distinction. A whole book—in the form of a generous quarto—was written about it by Dr. Herman Friedrich Kilian of Pesth, in 1822. I have read this work and as a result pay obeisance to Dr. Kilian and his scholarly exploitation of the ninth pair. Kilian shows that the history of this modest nerve is the history of early and modern anatomy.

The difficulties to be overcome in getting a full description of the glossopharyngeus, and its origin, distribution, anastomoses and function, were these: Prominent anatomists could not see it as a separate nerve, could not follow its course, or recognize its connections. When actually recognized, it was enumerated variously as the sixth pair, the fourth pair, the eighth pair, part of the seventh pair, etc.

The story of the research is told by Kilian and it is interesting, for it is unique historically and informing anatomically. Let me begin with his title page, which reads as follows: "Anatomical Studies of the 9th Pair of Cranial Nerves or the Glossopharyngeus with Notes Added from the Anatomical Museum of the University of Strassburg; Prepared by Dr. Herman Friedrich Kilian, Member of Several Learned Societies, with 2 Copper Plates. Pesth, 1822. Press of Adolph

Hartleben." The book is dedicated to his Excellency, H. B. Wilhelm von Popoff, State-Secretary and Knight of His Royal Majesty, Emperor of all the Russias, etc. And Kilian adds, "This work is a feeble evidence of good wishes shown the author." In this, one notes that Kilian gives us a human touch.

In the makeup of the book we are given the history of the anatomic researches and something of the lives of fifty-five human anatomists who have contributed to our knowledge of the cranial nerves. Most of these anatomists only described our nerve in part and gave information, or misinformation, according to their ability Kilian's story ranges from the time of Galen (A.D. 130) to that of Bichat, Meckel and himself in the early part of the nineteenth century.

He prefaces his tale with the wise and appropriate words of Seneca:[1] "Multum egerunt qui ante nos fuerunt, sed non peregerunt . . . post mille secula praescindetur occasio aliquid adjiciendi."

Dr. Kilian illustrates his own description of the nerve's anatomy with two full-page well drawn and colored illustrations. In using Kilian's work as I am doing, I am able not alone to present the history of the unfolding of the ninth pair of cranial nerves, but also to tell a little about the personality of some of the numerous eminent men who worked at it.[2]

The story of the ninth nerve is an interesting illustration of the long and laborious processes by which neural anatomy is developed. One may almost say that if one knows this book of Kilian's he knows not only all the anatomy of the cranial nerves but also the history of medicine.

I shall not inflict on the reader a detailed record of Kilian's work; I wish only to give through it some idea of the anatomic activity of the sixteenth, seventeenth and eighteenth centuries, and to indicate how hard was the work and long the time before our cranial nerves were known.

Dr. Kilian admitted that the various cranial nerves had been eagerly studied by previous anatomists and neurologists; but he found that even in his day something remained to be done for the ninth. And he intimated that this nerve had been rather badly treated by its students in the past. I have placed the following illustrations of such maltreatment in a series, not chronologically arranged but covering the period when modern anatomy began; viz., with Mundinus and extending to the nineteenth century.

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1. Seneca: de Scientiis: "Those who lived before us did much, but they did not do all. . . . A thousand ages after our day, opportunity for adding to knowledge will exist."

2. Curiously enough, no woman ever studied the glossopharyngeal nerve, though it is such a real factor in articulation.

Mundinus (1276-1326), calls the glossopharyngeus, the fifth pair; Piccolimi (about 1586), the eighth pair; Laurentius (1558-1609), the fourth conjugation, contributing to taste; T. Willis (1621-1675), the ramus prior of the seventh nerve; Columbus (1516-1559), a branch of the middle sympathetic ganglion; Palfyn (1650), the petit hypoglossal; Carl S. Andersch, living as late as 1797—"one of the most distinguished, industrious and intelligent of anatomists," says von Haller—in

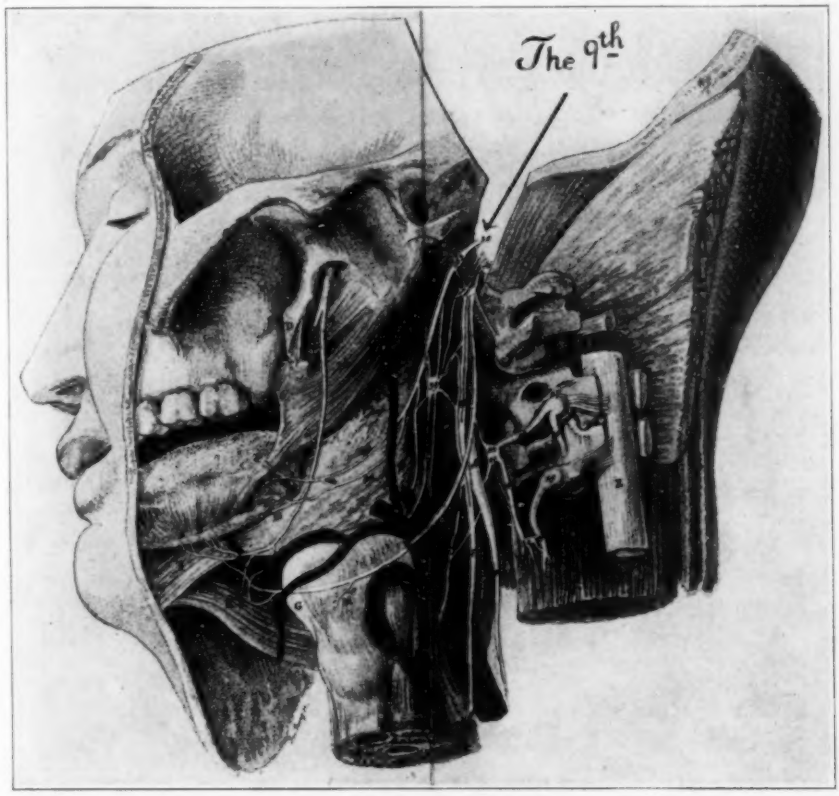

Fig. 1.—Reproduction from Kilian's "Monographie des neunten Hirnnervenpaares." The glossopharyngeal nerve is indicated by the arrow.

classifying and numbering the cranial nerves, makes the glossopharyngeal the eighth pair.

With these preliminary notes, I will give in small detail a record of some of the work and workers on the ninth pair from the time of Galen to that of Kilian. The interest in the account, I think, is not alone in the anatomic part but also, as already intimated, in its references to the character and personality of the men.

Galen (A.D. 130-200).—"I begin my chronologic record," says Kilian, "with the incomparable Galen, who had intimate knowledge of the glossopharyngeal, though he gave it no special name." Says Galen, describing the sixth pair of nerves: "These issue from the skull in three portions. Each of these has a distinct course, later mixing with other nerves." These three nerves recognized by Galen were the vagus, the glossopharyngeal and the accessory. He traces the glossopharyngeal to the muscles of the throat and tongue, and practically shows a much better knowledge of the pair than many later anatomists. Kilian attributes this to the fact that Galen dissected dogs and asses in which the glossopharyngeal is better differentiated than in man. Incidentally, I may say that Galen found and described seven pairs of cranial nerves.

Avicenna, the Persian (A.D. 980-1036).—Avicenna is quoted next as describing three cranial nerves issuing from the same foramen, and he distinctly states that one of them sends some fibers to the throat and others to the back part of the tongue. Avicenna is said by Arnaldus of Villa Nova to have been only "a professional scribbler" who stupefied European physicians with his prodigious volumes; viz., his "Canons" of Medicine "which are full of ingenious misinterpretations of Medicine." But he seems, so far as he went, to have described the glossopharyngeal nerve correctly—probably following Galen.

Mundinus of Luzzi (1276-1326).—Mundinus was a surgeon and anatomist. He was the first man of the renaissance to show anatomic initiative. He dissected the human body in public and wrote an anatomy which was the textbook for two centuries—the student "colet Mundinum ut Deum" says his historian. He described seven pairs of cranial nerves in curious order; the first is that of vision; the second, the motor oculi; the third, the facial; the fourth, which goes to the stomach and diaphragm, the vagus; the fifth, the auditory; the sixth, the glossopharangeal; the seventh, that "subtle nerve" the hypoglossus which goes to the palate and gives sensibility to that part.

Vesalius (1523-1564).—From the time of Mundinus (1276-1326) to that of Vesalius, four physicians of some importance wrote on anatomy. They were J. B. Carpus, A. Benedictus, J. Dryander and Jacobus Sylvius, teacher of Vesalius. None of these made any contribution to the cranial nerves. They are mentioned apparently on this account.

Kilian expected to find much about the ninth pair in Vesalius, he being already accredited the "Father of Anatomy"; but, as a matter of fact, neither the vagus nor the ninth nerve are well described or correctly depicted. Galen here was better informed than Vesalius.

Estienne (1564).—Estienne or Carolus Stephanus, to give his Latin name, was a surgeon, anatomist and printer of Paris. He published a

work on anatomy a little while after that of Vesalius (1545). It was and is still the most artistic and picturesque anatomy ever published, but he followed Galen rather closely. He describes the vagus, the ninth and the accessory nerve as forming the sixth pair. He describes the ninth as a separate branch of the sixth pair going to the throat and tongue, but both the description and his plate are inadequate. He incidentally described a spinal cord with syringomyelia.

Poor Stephanus was put in prison for heresy and died there.

Eustachius (1524-1574).—He lived and worked at the time of Vesalius. He gave no definite written description of the ninth pair, but his "Tabulae Anatomicae," published by Lancisi 100 years after the author's death, show, says Kilian, that "Our nerve for the first time is very well and correctly depicted. His knowledge of the distribution of the nerve was correct but not complete." Eustachius depicted, says Albinus, eight pairs of cranial nerves. It is important to know that Eustachius made his own dissections and his own drawings at Rome, but he was too poor to publish them. When they did appear, it was made apparent that in his anatomic knowledge he was ahead of his contemporaries. He probably was lacking in what is now called "pep," a quality that very much animated the Belgian Vesalius.

Gabriel Fallopius (1523-1562).—This physician was many-sided and most distinguished, gaining his education against great difficulties. He was professor of anatomy at Ferrara when only 25, then at Pisa and three years later at Padua. He was a critical observer and was rather especially critical of Vesalius. His work "Observationes Anatomicae" was published in 1561. He is credited with many original observations and discoveries partly because, it is said, he received the gift of criminals as anatomic subjects on whom he experimented in vivo. He is credited with poisoning and vivisecting these unfortunates. It was an old Alexandrian practice.

Fallopius described the motor eye muscles and demonstrated the cervical and lumbar swellings of the cord. His studies definitely promoted our knowledge of the nervous system, and his career arouses the enthusiasm of Kilian who gives to Fallopius many pages, and says that he first distinctly asserted the ninth to be a separate cranial pair. He showed that branches of this ninth communicated with the olivary ganglion, which he was the first to discover.

Fallopius described the tubes now called by his name. He lived to be only 39, but, our historian says, in the beauty of his personal character as well as in the amount and excellence of his anatomic work, he stands first of the Italian anatomists of his day. Fallopius, Eustachius and Vesalius make a notable sixteenth century trinity.

Felix Plater (1536-1614).—Plater was professor of medicine at Basel in 1560. He was a progressive and sound anatomist, a propagandist of the new methods and the first to dissect a human body in Germany. He was also the first systematic nosologist. He wrote an interesting account of student university life in his day and seems to have been a very human person. He never personally investigated the ninth nerve, but he describes it in his anatomy as the sixth pair.

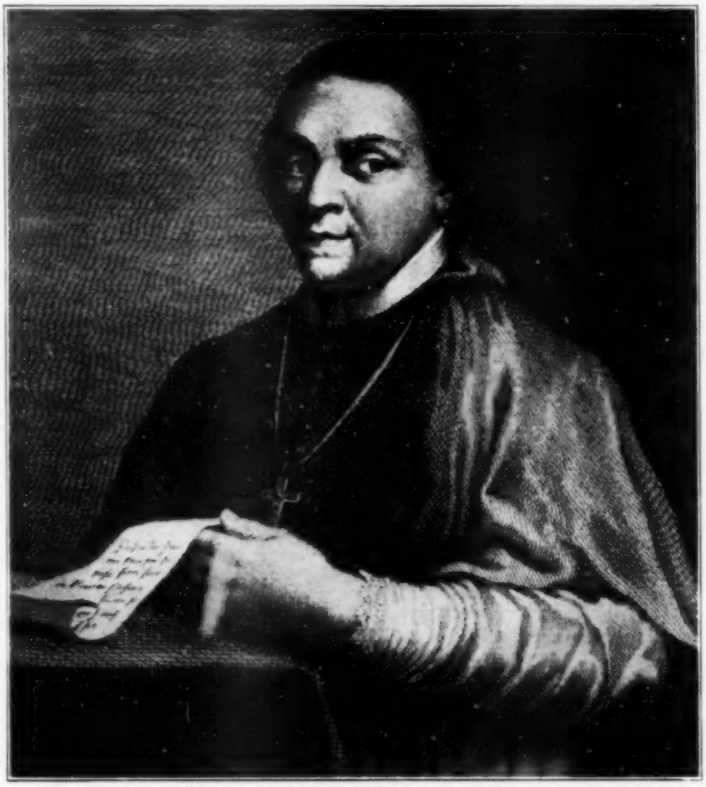

Fig. 2.—Vidus Vidius, 1569.

Constantinus Varolius (1543-1565).—He was a Spaniard, born in Bologna. He became professor of anatomy at Rome and papal physician. He died at the age of 32. Two anatomic works are ascribed to him, in one of which, "De Nervis, etc.," he described the Pons Varolii; but his anatomic description of the cranial nerves is incorrect and very poor. Kilian counts him a very bad anatomist, but he attained eponymic immortality in his short years.

Realdus Columbus (1516-1559).—Columbus has been much exploited as discoverer of the pulmonary circulation. He described this

imperfectly, and he probably got his idea of it from Servetus. However, he was one of the best and most observant of the followers of Vesalius, whose chair he took when Vesalius left Padua. He wrote a treatise on anatomy in which he corrected some mistakes of Vesalius and added observations of his own. He was the first to state that there were nine pairs of cranial nerves. He, however, does not recognize our ninth as a pair, but calls it the "dextur nervus" of the sixth pair, which he says sends fibers to the muscles of the larynx and to those of the tongue. He surpasses all other writers, says Kilian, in the clearness and correctness of his description of the cranial nerves.

He was rather nasty in his comments on Vesalius, according to Baas.

Vidus Vidius (1569).—We come now, says Dr. Kilian, to one of the most discriminating and important anatomists of his time, whose tireless industry and absorption in details brought precious fruits to the finer points of anatomy as shown, for example, in his description of the vidian nerve. As regards the ninth pair of nerves, we find that he described its origin and recognized its autonomy, but he did not follow its extracranial course with any especial care. Vidius was a Florentine, and his Italian name was Guili Guidi. He lived in Paris and organized the College of France. He was later a professor at Pisa. He was a friend of Benevenuto Cellini. His anatomic works were published by his nephew long after the author's death. It is curious that despite this he succeeded in passing into history.

Both Vidius and Fallopius (1584) make out eight pairs of cranial nerves, as follows: I, optic; II, oculomotor; III, trigeminus; IV, abducens; V, facial (communicans faciei); VI, acusticus; VII, vagus, glossopharyngeal and accessory; VIII, hypoglossus.

Archangelus Piccolominus (1526-1605).—Piccolominus makes the following classification of the cranial nerves: I, opticus; II, olfactorius; III, nervi motores oculorum; IV, nervi motores oculorem et partium circumjectarum; V., nervi gustatorii; VI, nervi auditorii; VII, nervi motores et sentientes interiorum partium et viscorum; VIII, nervi octavi conjugationis.

Kilian introduces him apparently only to denounce him as an absolutely ignorant and worthless anatomist. Still he was professor of anatomy at Rome and he is said to have "discovered" the linea alba!

A. Laurentius (1558-1609).—He was chancellor of Montpelier and physician to Henry IV of France. His writings lack clearness, says Kilian. He described seven pairs of cranial nerves, and made the glossopharyngeal the fourth: I, optic; II, oculomotor; III, gustatory; IV, glossopharyngeal; V, auditory, including part of the hypoglossus; VI, vagus; VII, hypoglossal. Laurentius published an "Anatomy"

(Paris, 1600). The frontispiece consists of a portrait of the author, a very ugly man. This fact does not prevent the formal Latinized announcement "You here see the countenance of Laurentius in which the fulness of his divine genius is conspicuous."

Isbandus Diemerbroeck (1695).—Diemerbroeck held that there were seven pairs of cranial nerves: I, optic; II, motor oculi; III, sense of

Fig. 3.—A. Laurentius, 1558-1609.

smell; IV, sense of taste; V, auditory; VI, vagus; VII, hypoglossus. He published his "Anatomia Corporis Humani" at Lyons in 1696. He chiefly copied the discoveries of others.

F. Ruysch (1638-1731).—Ruysch, a professor at Amsterdam, had a brilliant talent for making very fine anatomic preparations and is called "the famous inventor of minute injections." His name was well

known throughout Europe. He recognized the ninth, but did not regard it as a special nerve. (Opera anatomica, Amsterdam, 1721.)

We have gone over the records of only fifteen of the fifty-five anatomists studied by Kilian and we show that up to the middle of the eighteenth century the glossopharyngeal nerve was not universally recognized as a ninth pair and not completely and correctly described. It would be futile to go further with the story. Kilian gives us critical

Fig. 4.—Samuel Sömmering, 1755.

records and a bibliography telling of the remaining eminent and well known anatomists of the eighteenth century: Vieussens, Ridley, Morgagni, Winslow, Alex Monro, Von Haller, Wrisberg, Vicq D'Azyr, Sömmering, Bichat and, finally, Meckel. Kilian, at the end of his record, credits John Frederick Meckel, in his four-volume "Handbook of Human Anatomy," published in 1817, with giving the glossopharyngeus, "ein treues und ganz vollstandiges unenstelltest Bild."

Nearly all of the men whose descriptions are quoted and critically examined had written textbooks of anatomy, and Kilian's monograph is thus a real contribution to the bibliography of anatomy with a portentous emphasis on the ninth pair of cranial nerves.

After going over some of the present day works on the glossopharyngeus, I am inclined to feel that the nerve even yet deserves anatomic and physiologic study. The two elaborate works on the human cranial nerves by Flower, 1880, and Hughes, 1902, do not absolutely agree and are not physiologically complete. The latest, and I presume most authoritative, work with which I am familiar is that by Hudson Herrick in Wood's "Handbook" (1910). He uses the term "probably" in his description of it and he certainly does not seem to claim finality. According to Dr. Herrick, in his description of this nerve, it contains:

1. Somatic afferent sensory fibers for tactile sense to the posterior one third of the tongue. The jugular ganglion belongs to this component which gets fibers from the spinal tract of the fifth nerve and ends in the spinal fifth nucleus.

2. Unspecialized visceral afferent sensory fibers from the sympathetic system which end in the nucleus of the fascicularis solitarius.

3. Afferent gustatory fibers from the posterior third of the tongue. Parts 2 and 3 are related to the ganglion petrosum and end in the nucleus of the fascicularis solitarius.

4. Efferent fibers of two kinds: (*a*) One set arises from the nervus ambiguus and goes to the stylopharyngeus muscle. These are of specialized visceral motor type, going to the striated muscles. They form the greater part of the efferent system. (*b*) There are less numerous fibers which go to the sympathetic preganglionic neurons. They are excitoganglionic. They go in the tympanic branch of the ninth and innervate the parotid. They arise from the nucleus salutorius inferior near the rostral end of the nucleus ambiguus. (*c*) Other efferent fibers are for unstriped muscles and arise from the dorsal vagus nucleus.

It follows that the ninth nerve gives tactile and special sense to the posterior one third of the tongue and gives some visceral sensation to the throat. It gives motion to the stylopharyngeus, and these fibers form the mass of the efferent system. It stimulates the salivary secretion, and gives a few motor visceral fibers.

I have had some clinical experiences which lead me to doubt some of Herrick's statements. And I have been led to think that the functions of this nerve may vary, especially as regards the sense of taste and the supply to the middle ear. In origin and distribution the nerve is a very close cousin to the vagus. I am not sure that Willis is not right and that biologically and phylogenetically the ninth, tenth and bulbar eleventh are really one nerve.

It is but just to Kilian to enumerate the names of the anatomists whose work and life he carefully presents. They are:

Claudius Galen
Avicenna
Mundinus
Andreas Vesalius
Carolus Stephanus
Realdus Columbus
Gabriel Fallopius
B. Eustachius
Vidus Vidius
Felix Plater
A. Piccolominus
G. Bauhinus
J. Riolan
A. Spiegel
G. Rolfink
A. Laurentius
Bartholin
Thomas Willis
G. Blasius
F. Ruysch
I. Diemerbroeck
J. G. Duverney
G. Bidloo
R. Vieussens
P. Verheyen
H. Ridley
J. Palfyn
J. O. Sautorini
William Cheselder
J. B. Morgagni
J. B. Winslow
A. F. Welcker
Alexander Monro
Albrecht von Haller
C. A. von Bergen
Joseph Lieutand
J. van Revenhorst
J. B. Bonhomme
P. Martin
George Coopmanus
D. Cotunne
H. A. Wrisberg
Sabatier
A. Portal
F. Vicq D'Azyr
S. P. Sömmering
C. T. Andersch
J. G. Haase
Bichat
A. Boyer
J. C. Rosenmiller
J. F. Meekel.

HUMAN ADULT AND EMBRYO ANTERIOR HORN CELLS

A COMPARISON OF FORM IN RELATION TO THE CONCEPT OF NEUROBIOTAXIS *

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AND
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NEW YORK

CONTENTS

INTRODUCTION

In a preceding paper [1] one of us has shown with Lhermitte that the longest diameter of the motor cells of the anterior horn of the adult human spinal cord is in the cephalocaudal axis of the spinal cord and that this diameter is twice or more than twice the length of the dorsoventral and dextrosinistral diameters.

At first sight this fact seems only of morphologic significance, only of importance in changing in textbooks of the anatomy of the nervous system the idea of the form of these cells by pictures of their three dimensions.

If, however, we inquire more deeply into the details of this problem, we recognize that these new facts may furnish some new ideas about the relations between cellular form and function, and that something may be added to one of the foundations of modern neurology, the theory of neurobiotaxis.

It is to Ariens Kappers,[2] that we owe a wider conception of the problem of neurobiotaxis. He recognizes the priority of Ramón y Cajal [3] who in 1893 had published the theory that the formation of the nervous system follows certain physical and chemical laws. Cajal's conception was that the production of repelling and attracting chemical substances by two nerve cells was the reason for their relation and for

* From the Neuropathological Laboratory, Montefiore Hospital.

1. Lhermitte, J., and Kraus, W. M.: On the Form of the Anterior Horn Cells, Anat. Rec. **31**:123 (Oct.) 1925.

2. Kappers, C. U. A.: On Structural Laws in the Nervous System: The Principle of Neurobiotaxis, Brain **44**:125 (July) 1921. (Reference should also be made to preceding publications.)

3. Cajal, Ramón y: La rétine des vertébrés, Cellule **9**:119, 1893.

the formation of the dendrites. Kappers pointed out that the question whether two neurons are connected by protoplasmic bridges (persisting "plasmodesms," according to Hensen and Sedgwick,[4] or persisting embryonic syncytium according to Cunningham [5]) is of minor importance compared with the other question whether the relations between neurons are arbitrary or follow distinct laws. He himself thinks that the organization of the nervous system may be explained by bio-electrical laws; and his reasons for these ideas are found in investigations of the chemistry of the nervous system. One of us [6] has proved several times that the differences in the chemical make-up of nerve fibers and nerve cells are significant enough to support, to a certain extent, the theories of different bio-electrical potentials in these two parts of the neurons.

Kappers [7] started, however, from his comparative anatomic studies, by which he proved that during phylogenesis and following certain biotactic laws certain nuclei in the brain change their positions fundamentally. He formulated the laws of neurobiotaxis in the following sentences:

1. If in the nervous system several stimulation-changes occur, the growth of the chief dendrite, and eventually the displacement of the cell-body itself takes place in the direction whence the majority of stimuli proceed to the cell.

2. Only between correlated centers does this outgrowth or shifting take place.

3. The growth of the axis-cylinder (i. e., its final connection) is not primarily regulated by motor centers, but also here synchronic or successive stimulation (correlation) acts a part.

If we apply these laws to the form of the motor cells of the anterior horn of the human cord, we should find that:

1. (*a*) The form of the cell is determined by the direction "whence the majority of stimuli proceed to the cell." (*b*) The longest diameter of the cell corresponds to the direction in which the strongest stimuli pass to the cell.

2. The form of the cell indicates the direction and strength of the stimuli acting on it and the situation of correlated centers.

3. The axon of the cell runs in the direction of the longest diameter.

4. Sedgwick, A.: On the Inadequacy of the Cellular Theory of Development and on the Early Development of Nerves, Particularly of the Third Nerve and of the Sympathetic in Elasmobranchii, Quart. J. Micr. Sc. **37**:87-102 (Nov.) 1895.

5. Cunningham, D. J.: Textbook of Anatomy, ed. 5, New York, William Wood and Co., 1918, p. 504.

6. Weil, Arthur: Die Quellung von Rinde und Leitungsbahnen des Grosshirns als Funktion ihres chemischen Aufbaus, Pflüger's Arch. f. d. ges. Physiol. **179**:21-49 (Feb.) 1920.

7. Kappers, C. U. A.: Further Contributions on Neurobiotaxis, J. Comp. Neurol. **27**:266 (April) 1917.

THE ADULT CELL

Lhermitte and Kraus have already proved that the longest diameter of the anterior horn cells in the different segments of the cord is in the cephalocaudal axis. In order further to confirm these facts, we have reconstructed in wax from series of longitudinal sections of the cord the three types of cells. These correspond to the models formerly produced from transverse sections. Finally we have reconstructed three hypothetic cells by combining a transverse model with the ends of a longitudinal one.

We desire to point out that the best way to proceed is to begin with the drawing of an isolated group of several cells at magnification of about 150 diameters and to continue this through five or six following sections.

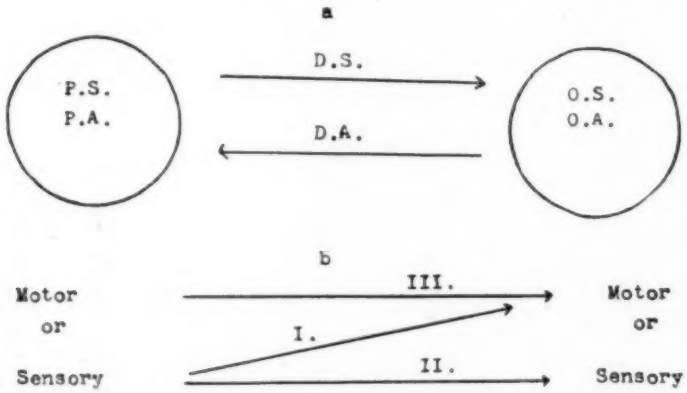

Fig. 1.—*a*. The object (nucleus, cell) is attracted to the P.S. or P.A.; applied to the cell form, the cell is elongated in the direction of and toward points of stimulation (or attraction). P.S. indicates point of origin of stimulation, which is the same as P.A., point of origin of attraction; O.S. indicates object of stimulation, which is the same as O.A., object of attraction; D.S. indicates direction of stimulation, which is opposite to D.A., direction of attraction. *b*. There may be attraction (in the opposite direction to that of the arrows, which indicates the direction of stimulation) between two motor centers (III) and two sensory centers (II), as well as sensory and motor centers (I).

After this a system of lines is drawn which has its origin in a connecting line between two arteries and the larger cells. Then perpendicular lines are drawn 0.5 cm. apart on these lines. In this way we get a network of lines which will help to find the corresponding elements in successive sections, and also in drawing the cells at higher magnifications.

In addition to these reconstructions we have measured the average diameters for a large number of cells seen in transverse and longitudinal sections. The cells were drawn with the Zeiss-Abbe camera lucida at a magnification of 600 diameters. We took only cells whose Nissl bodies were well stained and which contained the nucleus. We have already referred to the technic of the measurement in the preceding publication.

At first we have measured in transverse sections the longest diameter that divides the cell body into two equal parts and which corresponds to diameter 1 in the following tables. Diameter 2 runs perpendicular to diameter 1 and is not as long. Diameter 3 is the longest diameter in longitudinal sections and corresponds approximately to the longest cephalocaudal diameter of the cells.

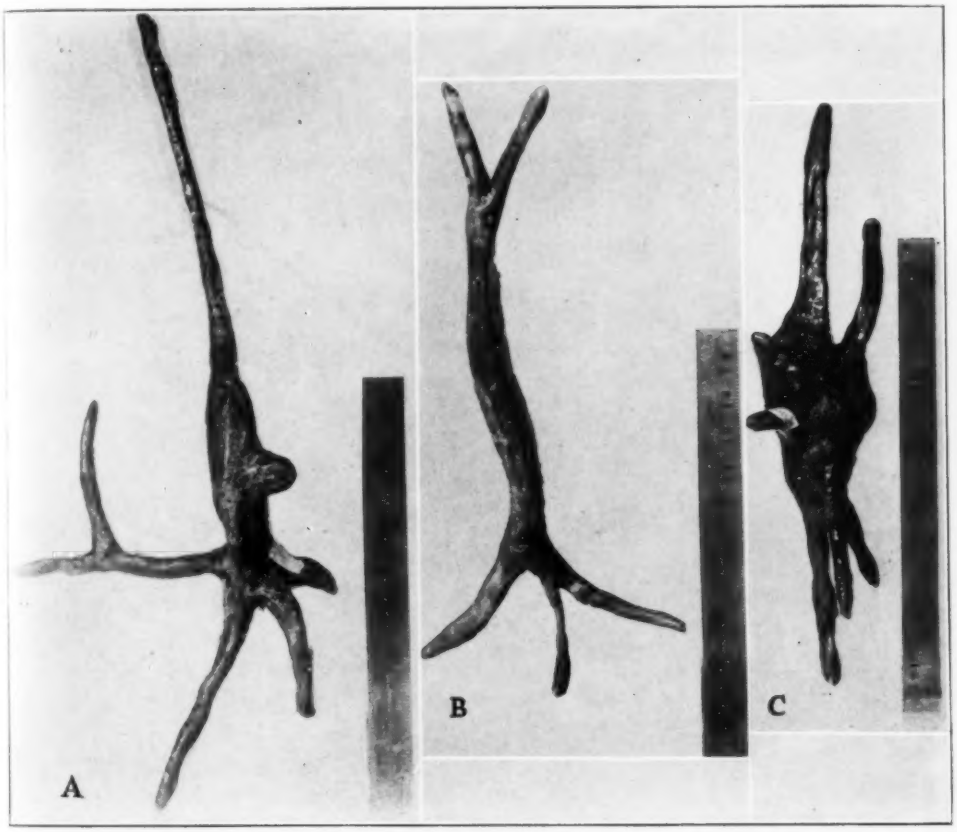

Fig. 2.—Reconstructions from longitudinal sections of anterior horn cells; 600 ×. The view is in the dorsoventral direction; *A*, segment cervical 5; *B*, segment thoracic 6; *C*, segment lumbar 4.

The descriptions of the size of the anterior horn cells found in the literature give only a very incomplete idea of their form; the measurements are only for transverse sections. Ziehen [8] gives the following for the largest diameters of the largest cells: upper cervical segments, 40

8. Ziehen, T.: Nervensystem in von Bardeleben, K.: Handbuch der Anatomie des Menschen, Sections 1-3, Centralnervensystem, Part 1, Jena, Fischer, 1899, p. 130.

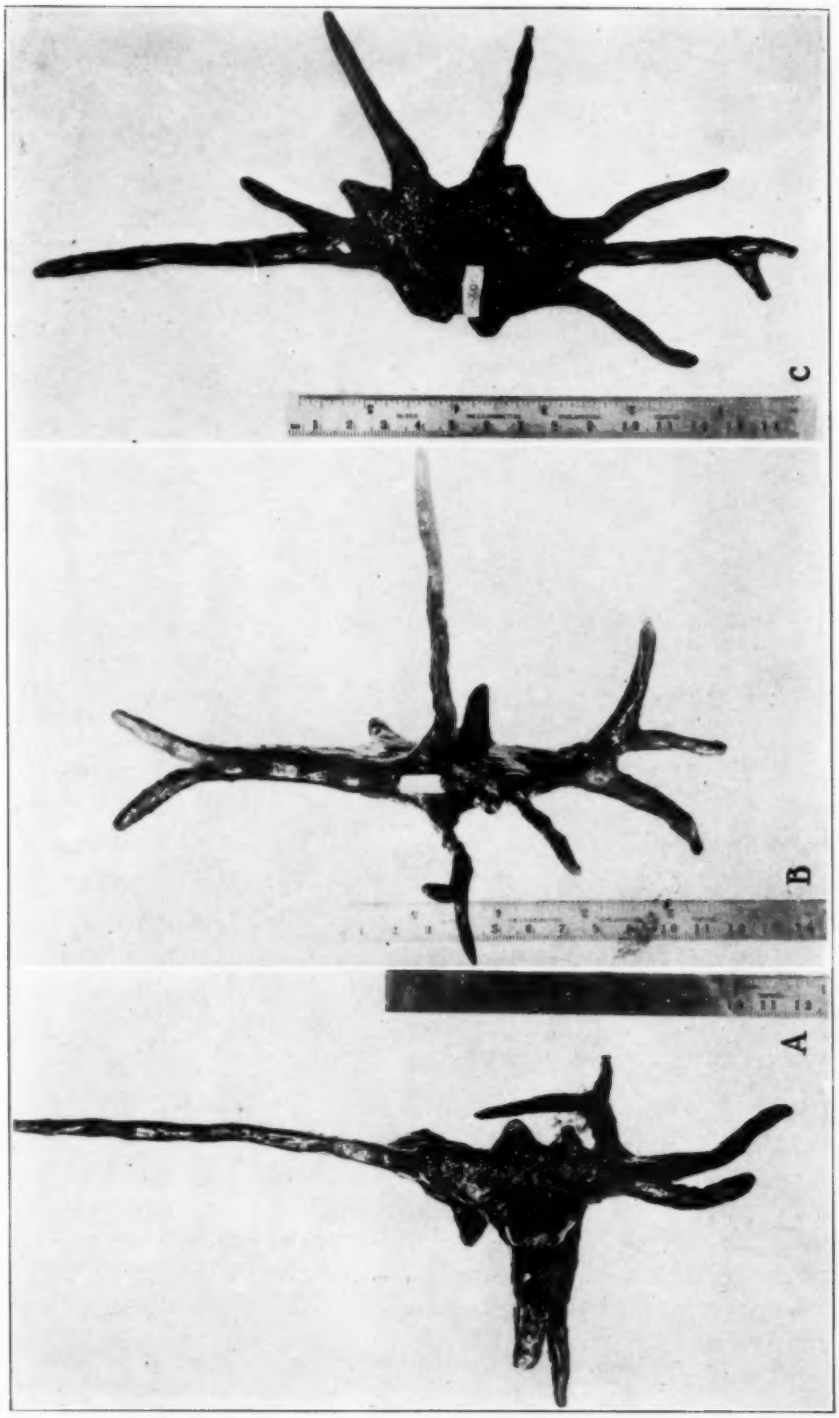

Fig. 3.—Reconstruction from combined longitudinal and transverse sections of anterior horn cells; 600 ×. *A*, segment cervical 4-5; *B*, segment thoracic 5-6; *C*, segment lumbar 4.

microns; cervical enlargement, 82 microns; middle thoracic segment, 63 microns; lumbar enlargement, 70 microns.

According to Koelliker,[9] the diameter is from 67 to 135 microns; the cells of the dorsomesial groups are smaller, from 30 to 80 microns. The size is independent of the length of the person's body. In the

TABLE 1.—*The Three Different Dimensions of the Adult Anterior Horn Cells: Averages, Measured in Microns* *

Group	Cervical 4 and 5			Thoracic 5 and 7			Lumbar 4		
	2	1	3	2	1	3	2	1	3
Intermediate dorsolateral	21	41	79	—	—	—	—	—	—
Dorsolateral	28	51	88	—	—	—	35	50	85
Ventrolateral	24	51	104	—	—	—	35	62	74
Dorsomesial	20	32	70	12	27	80	16	32	67
Ventromesial	18	33	64	21	34	85	32	53	75

* In this and the following tables, 1 indicates the longest diameter in transverse sections; 2, the diameter perpendicular to 1; 3, the longest diameter in longitudinal sections.

TABLE 2.—*The Three Different Dimensions of the Adult Anterior Horn Cells: Maxima*

Group	Cervical 4 and 5			Thoracic 5 and 7			Lumbar 4		
	2	1	3	2	1	3	2	1	3
Intermediate dorsolateral	33	67	97	—	—	—	—	—	—
Dorsolateral	37	72	101	—	—	—	40	82	97
Ventrolateral	35	91	140	—	—	—	38	82	101
Dorsomesial	33	45	80	17	37	112	21	30	76
Ventromesial	35	47	100	33	47	120	45	68	87

TABLE 3.—*The Dorsoventral and Dextrosinistral Diameters of the Adult Anterior Horn Cells*

Group	Cervical 4 and 5				Thoracic 5 and 7				Lumbar 4			
	Averages		Maxima		Averages		Maxima		Averages		Maxima	
	Dorsoventral	Dextrosinistral	Dorsoventral	Dextrosinistral	Dorsoventral	Dextrosinistral	Dorsoventral	Dextrosinistral	Dorsoventral	Dextrosinistral	Dorsoventral	Dextrosinistral
Dorsolateral	29	49	37	70	—	—	—	—	40	42	47	53
Ventrolateral	27	48	43	68	—	—	—	—	50	47	67	67
Dorsomesial	24	19	42	33	14	20	20	27	18	18	27	25
Ventromesial	24	27	47	38	28	27	43	37	48	43	60	52

classification of the different groups we have followed the nomenclature of Tilney and Riley.[10]

Diameters 1 and 2 do not always correspond to the dextrosinistral and dorsoventral diameters. Most of the largest diameters of the cells

9. Koelliker: Handbuch der Gewebelehre, ed. 6, Leipzig, W. Engelmann, 1902, p. 61.

10. Tilney, Frederick; and Riley, H. A.: The Form and Function of the Central Nervous System, New York, Hoeber, 1921.

in transverse sections have a more or less oblique position to these two diameters. Table 3 may illustrate these facts by giving the averages and maxima of the dorsoventral and dextrosinistral diameters in transverse sections of the adult cord.

Fig. 4.—Adult anterior horn cells in longitudinal section, stained with toluidin blue; segment thoracic 5-6; 150 ×.

From these measurements in table 3 and from the reconstructions the following conclusions have been drawn:

1. (*a*) The form of the cell is determined by the direction "whence the majority of stimuli proceed to the cell." (*b*) The longest diameter of the cell corresponds to the direction in which the strongest stimuli pass to the cell.

2. (*a*) The form of the cell indicates the direction and strength of the stimuli acting on it and the situation of correlated centers. (*b*) Correlating centers whose stimuli originate in the more caudal and cranial segments produce the elongation in the cephalocaudal plane. Judging from the size and the form of the dendrites these intersegmental stimuli seem to be more powerful than the intrasegmental ones. (*c*) According to the law of the resolution of forces, the form of the cell depends

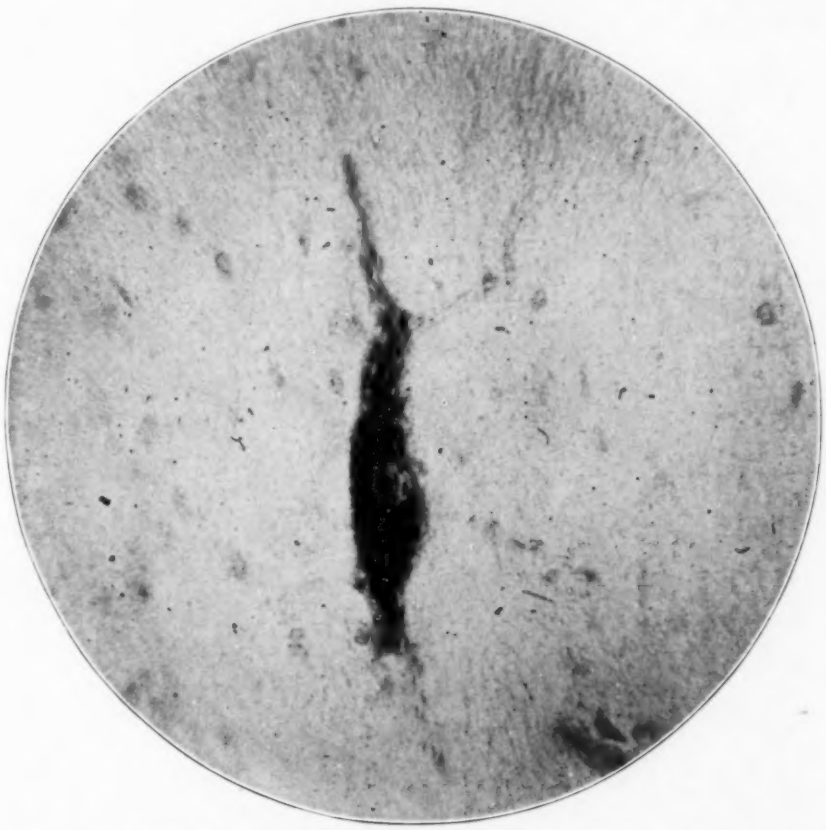

Fig. 5.—Adult anterior horn cell in longitudinal section, stained with toluidin blue; segment thoracic 5-6; 600 ×.

on the direction whence the different stimuli proceed; i. e., in a given plane the longest diameter is the diagonal of the parallelogram of forces which stimulate the cell body in this particular plane.

3. The axon does not run in the direction of the longest or cephalocaudal diameter, but perpendicular to this direction which is contrary to the previous conclusion that the axon of the cell runs in the direction of the longest diameter.

THE EMBRYO CELL

After determining the form of the adult anterior horn cell, we studied the development of this cell in the embryo. The cord of a 4 month old embryo (vertex-breech length = 125 mm.; vertex-heels = 211 mm.) was used. The age was determined from the tables of Keibel and Mall.[11] This age was chosen because there is no myelination and because the cells are differentiated enough for drawing purposes.

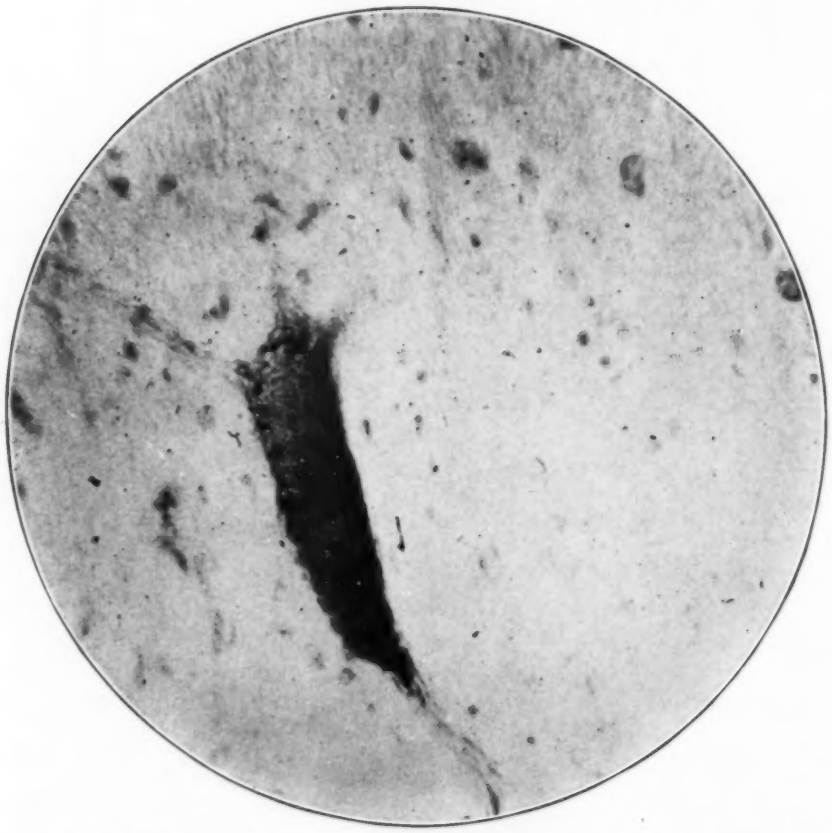

Fig. 6.—Adult anterior horn cell in longitudinal section, stained with toluidin blue; segment cervical 5; 600 ×.

The literature on this special subject is not very extensive. A table of maximum and minimum numbers of different ages is given by Kaiser and quoted by Ziehen [12] in which the transverse diameters for the lateral groups of anterior horn cells have the following averages: fetus

11. Keibel, F., and Mall, F. P.: Manual of Human Embryology, Philadelphia and London, J. B. Lippincott Company, 1910.

12. Ziehen (footnote 8, p. 131).

in the beginning of the fifth month, from 16 to 27.5 microns; in the beginning of the sixth month, from 17 to 33 microns; in the beginning of the seventh month, from 23 to 44.5 microns; in the beginning of the eighth month, from 23 to 48 microns; new-born, from 17.5 to 53 microns; at the age of 15 years, from 26 to 53 microns; adult, from 23 to 59 microns.

In order to compare the embryonic cells with the measurements which are given in tables 1 and 2, the same diameters of the transverse and longitudinal sections in different segments of the cord of the 4 month old embryo were taken.

TABLE 4.—*The Three Different Dimensions of the Anterior Horn Cells of a Four Month Human Embryo: Averages Measured in Microns*

Spinal Segments Opposite Vertebrae	2	1	3
Cervicals 1 to 7	19	—	23
Cervical 8 to thoracic 1	18	22	—
Thoracics 2 to 5	15	22	25
Thoracics 6 to 7	13	20	25
Thoracic 8	15	22	28
Thoracic 9	15	25	28
Thoracic 11—mesial group	17	22	25
Thoracic 11—lateral group	22	30	28
Thoracic 12	15	27	—

TABLE 5.—*The Three Different Dimensions of the Anterior Horn Cells of a Four Month Human Embryo: Maxima*

Spinal Segments Opposite Vertebrae	2	1	3
Cervicals 1 to 7	26	—	30
Cervical 8 to thoracic 1	24	28	—
Thoracics 2 to 5	20	27	30
Thoracics 6 to 7	18	23	33
Thoracic 8	17	28	30
Thoracic 9	25	38	33
Thoracic 11—mesial group	20	33	33
Thoracic 11—lateral group	25	38	35
Thoracic 12	20	33	—

A review of tables 4 and 5 shows that even in the anterior horn cells of the 4 month embryo the effect of the stimulating forces can be recognized. In all groups, except thoracic 11 and thoracic 12, the cephalocaudal diameter is the largest. The second largest is in most of the cells approximately the dextrosinistral direction. In longitudinal sections at a magnification of 1,200 diameters it may be seen that a number of cells in the different planes regularly form groups of their own whose dendrites go in a longitudinal direction (comparison should be made with fig. 10, *a*). In this way the shape of the single cell resembles that of a pear. Between these groups there are larger multipolar cells whose dendrites go in different directions, which therefore, are also subject to intrasegmental stimuli.

COMPARISON BETWEEN THE EMBRYO AND ADULT CELL

It is striking that the relations of the dorsoventral diameter 2 and the dextrosinistral 1 of the ventromesial cells of both the embryo and the adult are closely within the limits of the ratio of 1 : 1.2 and 1 : 1.8, while the craniocaudal diameter 3 of the adult cell is from two to three and a half times larger than the same diameter 3 of the embryo cell. Table 6 illustrates these facts.

Fig. 7.—Embryonic anterior horn cells in longitudinal section; spinal segment opposite vertebra cervical 8-thoracic 1; 250 ×.

According to the conception of neurobiotaxis, these findings would mean that during ontogenesis after the fourth embryonic month, the caudal and cranial stimuli become stronger than the dorsoventral and dextrosinistral; further, that with the progressive growth of the cells the equilibrium between the different pulls within the transverse sections of the thoracic segments is about the same in the adult as in the embryo. The embryonic cells show the formation of dendrites in different directions in the transverse sections at a magnification of about 1,200 diameters.

Most of the dendrites of the embryo go in only one direction of the longitudinal axis, either caudad or cephalad, while the stimuli acting during a later time of ontogenesis form dendrites in both of these directions of the longitudinal axis.

It would not be difficult to adapt the formation of the caudal and cranial dendrites to Kappers' theory, because we can suppose that correlating centers of the adjacent segments are producing the attracting stimuli of the caudal or cranial dendrites.

An illustration of the development of the embryonic cells into the different types of the adult anterior horn cells may be given by the

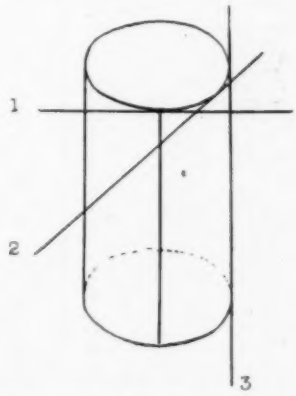

Fig. 8.—The different plans of cutting through an embryonic cord with reference to the drawing in figure 9; *1* indicates transverse sections; *2*, 45 degrees to horizontal plane; *3*, longitudinal sections.

TABLE 6.—*Relations of the Three Diameters Calculated from the Averages of Tables 1 and 3*

Parts of Cord Opposite the Following Vertebrae	Adult Cells: Dorsomesial Group			Adult Cells: Ventromesial Group			Embryonic Cells		
	2	1	3	2	1	3	2	1	3
Cervical 4 (cervicals 4 and 5)*	1	1.6	3.5	1	1.8	3.6	1	1.2	1.3
Thoracic 5 to thoracic 6 (thoracics 5 to 7)	1	2.2	6.7	1	1.7	4.5	1	1.5	1.9
Thoracic 11 (lumbar 4)	1	2	4.2	1	1.7	2.3	1	1.3	1.5

* To make possible a comparison between embryonic and adult cells, the parts of the adult cord have been labeled according to the vertebrae opposite which they lie. The actual cord segments in the adult are indicated in parentheses. The relations of the following numbers have been obtained by taking diameter 2 (dorsoventral) as the unit, thus showing the relations of diameter 1 (dextrosinistral) and diameter 3 (craniocaudal) to this first diameter.

drawings in figure 11, which represent the average measurements of the diameters in tables 1 (ventromesial and dorsomesial groups combined) and 4, at an enlargement of 1,000 diameters.

From these drawings we may conclude that the embryonic cells show the same differences in size in the three parts of the cord, cervical,

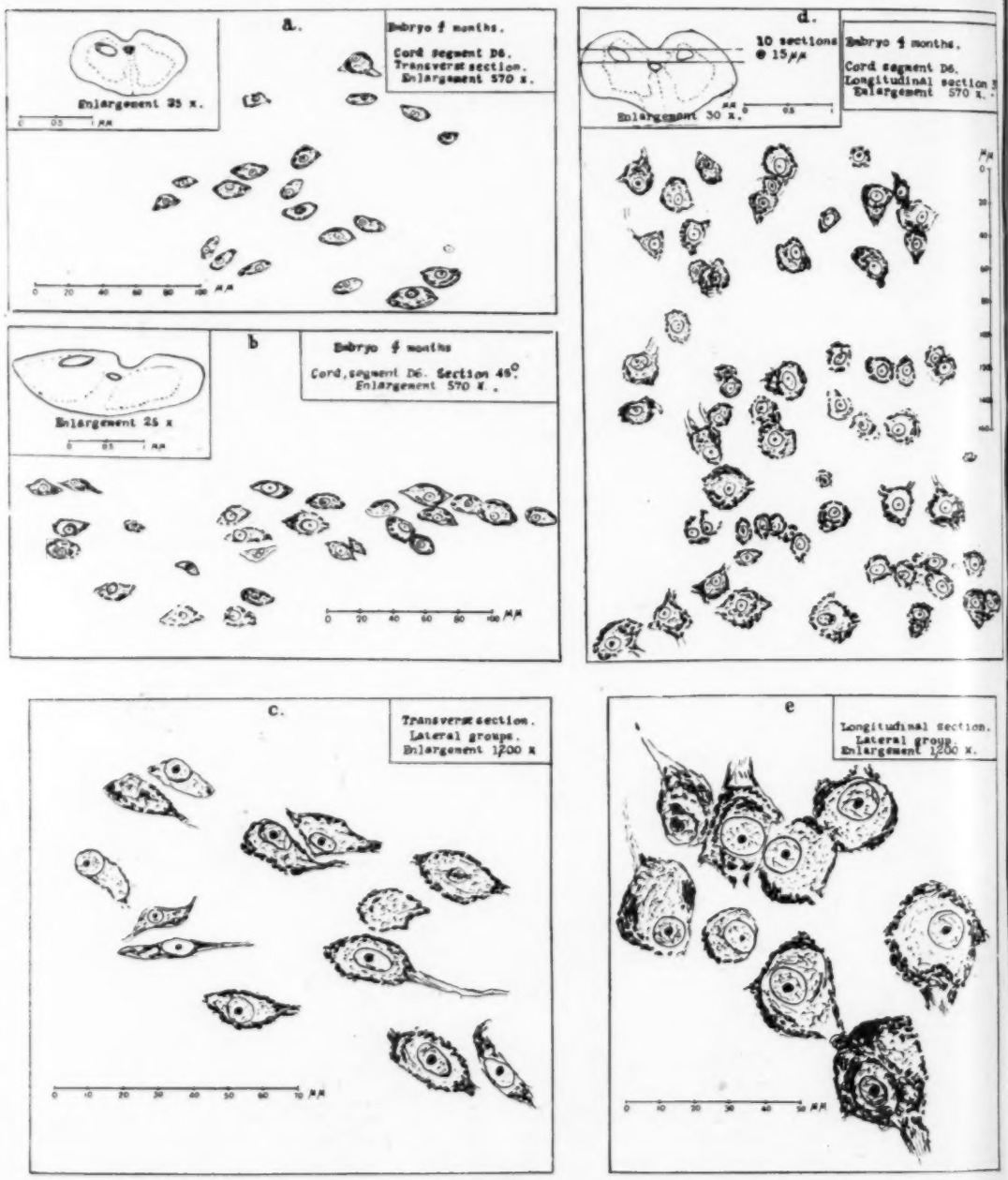

Fig. 9.—Camera lucida drawings of embryonic anterior horn cells: spinal segments opposite vertebra thoracic 6. *a*, drawing from plane 1, figure 8; *b*, drawing from plane 2, figure 8; *c*, lateral groups in plane 1, 1,200 ×; *d*, drawing from plane 3, figure 8; *e*, lateral group of plane 3, 1,200 ×.

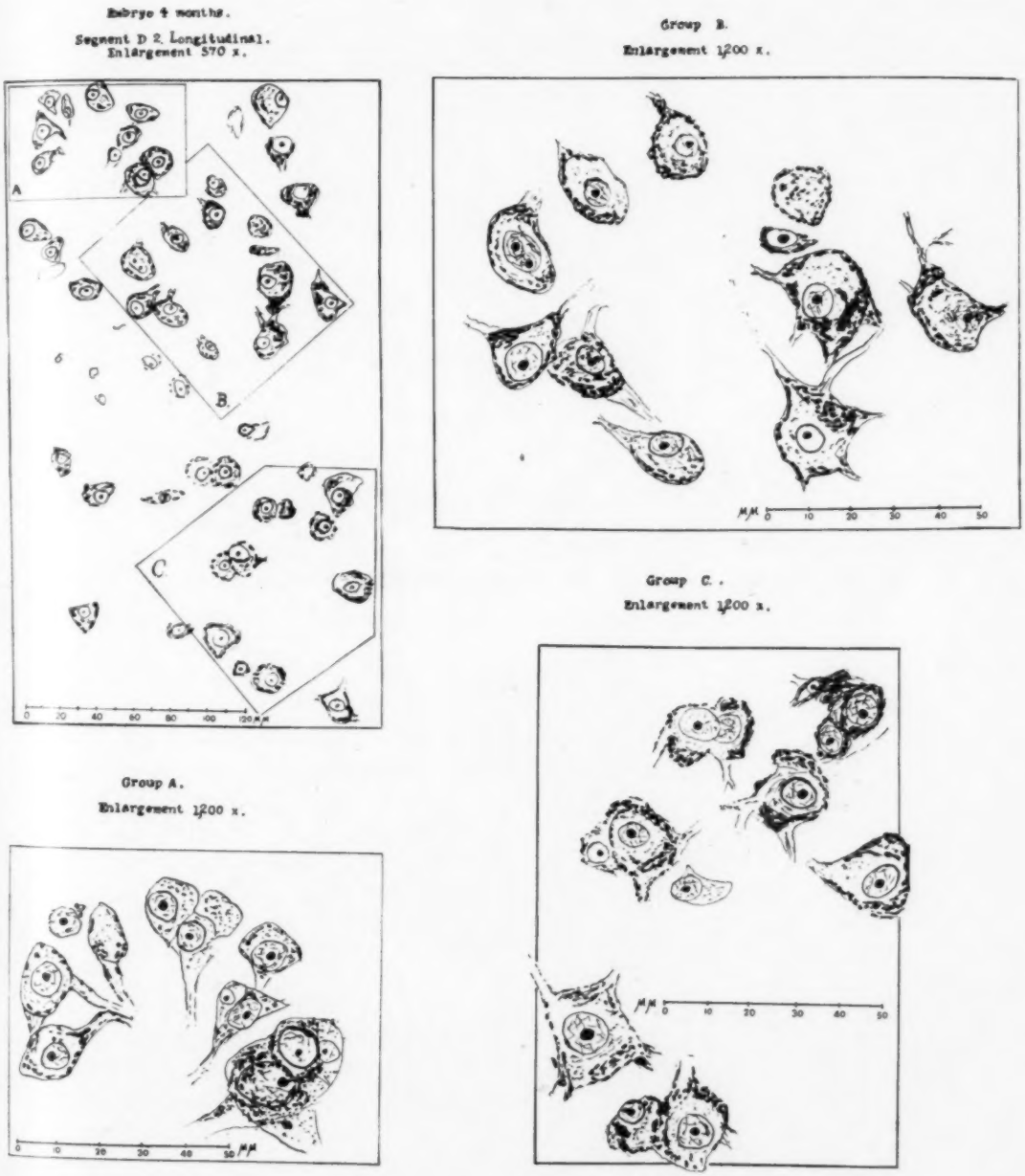

Fig. 10.—Camera lucida drawings of embryonic anterior horn cells in longitudinal section; spinal segment opposite vertebra thoracic 2; three different groups (*A*, *B* and *C*) to show the formation of dendrites, 1,200 ×.

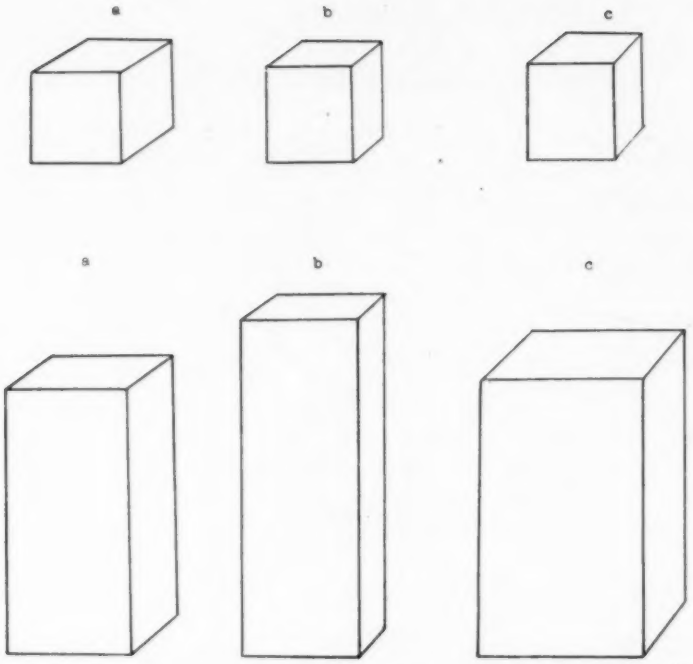

Fig. 11.—Average measurements of the diameters in table 1 (ventromesial and dorsomesial groups combined) and table 4 to show the difference between cervical, thoracic and lumbar cells. Upper row, embryonic cells; lower row, adult cells; *a*, cervical segment; *b*, thoracic segment; *c*, lumbar segment.

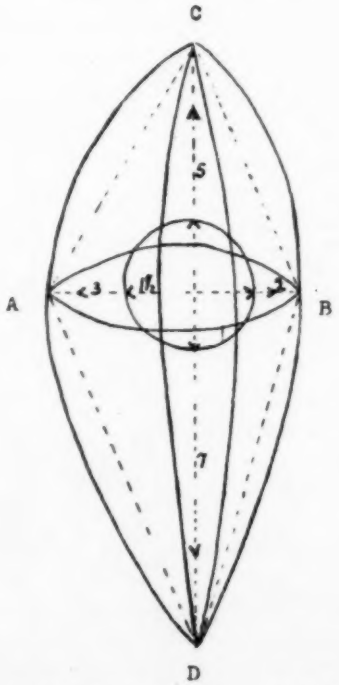

Fig. 12.—To illustrate the rôle of attraction by afferents on cell form: the circle represents the embryo cell; if pulls develop in the horizontal plane, the cell will become fusiform in that plane, *A-B*; if in the vertical plane, *C-D* results; a combination produces the cell form *A B C D*.

thoracic and lumbar, as they do in the adult, the range being in both embryo and adult: lumbar > cervical > thoracic. At the same time they emphasize again the fact that diameter 2, that is, the smallest diameter, remains nearly constant in embryo and adult and that the main change is the enlargement in the longitudinal axis.

CONCLUSIONS

1. The anterior horn cells of the spinal cord of a 4 month embryo and the adult cells resemble one another in the following respects: The cephalocaudal diameters of the cell bodies are the longest and the corresponding dendrites the largest. The proportions of the two transverse diameters to each other are almost the same. At both stages of ontogenesis, the order of size of the cells in the three different parts of the cord is lumbar >cervical > thoracic.

2. During ontogenesis the cephalocaudal axis elongates from two to three times more than the dorsoventral or dextrosinistral diameters.

3. The direction of the longest diameter is parallel to the long axis of the cord.

4. In the conception of the theory of neurobiotaxis, these findings would prove that: (*a*) During the fourth embryonic month, strong intersegmental stimuli, both cranial and caudal to the cell body, are responsible for its form and for the development of the longitudinal dendrites. These stimuli gain in strength during ontogenesis and finally produce the fusiform adult anterior horn cells. (*b*) Besides these stimuli other secondary stimuli are at work within the segments as early as the fourth month, but they do not increase in the same proportion as the intersegmental stimuli. (*c*) The stimuli regulating the growth of the axis cylinder direct it perpendicularly to the direction of the longest or cephalocaudal diameter. (*d*) *The afferents to cells determine their form, just as, according to the theory of neurobiotaxis of Kappers, afferents to nuclei determine their position.*

A CASE OF CERVICODORSAL SPINA BIFIDA OCCULTA

WITH TROPHIC AND SENSORY DISTURBANCES AND CERVICAL HYPERTRICHOSIS *

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Cases of cervical spina bifida occulta, with and without trophic disturbances, although not frequent, are well known in the literature. The following case, however, is worthy of publication because of the great extent and unusual site of the trophic disturbances.

REPORT OF CASE

History.—C. A., a boy, aged 10½ years, was the second child in a family of five, the first having died of meningitis at the age of 7½ months; the other three children are living and in good health. A brother of the mother formerly suffered with epileptic convulsions. The patient, born at term, presented at birth a cervicodorsal rhachischisis which extended upward and forward to the two fontanels and downward to the ninth dorsal vertebra, together with an area of intense pigmentation extending from the nape of the neck to the lower angles of the scapulas and covering the entire scapular region on both sides. At the age of 9 months, pustules began to appear on the elbows and forearms, which broke and discharged purulent fluid; sores followed, which in time formed eschars. Toward the end of the first year, similar pustules appeared on the hands. From that time there was a continuous series of pustules, all running the same course in a cycle of about two weeks, confined to the upper extremities and closing spontaneously. At the age of 6 years, following one of the pustules, necrosis occurred in the ungual phalanx of the second finger of the right hand; this spread to the other fingers of both hands and resulted in the spontaneous amputation of these phalanges. The trophic lesions had been painful until recently, when the patient ceased to complain of discomfort in connection with them, though they continued to appear in the same cycles. The cervicodorsal breach slowly and progressively closed from the first months of life, until, at the age of 10½ years, when the patient entered the clinic, there remained nothing more than a palpable fissure in the cervical region.

General Examination.—The height was 1.30 m. The cranial measurements were: anteroposterior diameter, 185 mm.; maximum transverse diameter, 145 mm.; maximum circumference, 545 mm.; anterior semicircumference, 265 mm.; posterior semicircumference, 280 mm.; bifrontal diameter, 98 mm.; bizygomatic diameter, 106 mm.; bigonial diameter, 87 mm.; occipitomental diameter, 192 mm. The cranial index was 0.78.

The skull was of pentagonoid, dolichocephalic type, with plagiocephaly; the parietal convexity was more marked on the left than on the right. The palatal arch was high and narrow.

A bifurcation of the vertebrae was felt extending from the nape of the neck to the fourth dorsal vertebra. The spinous apophyses could not be felt; where

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* From the Neuropsychiatric Department of the University of Rome.

they should have been was a lozenge-shaped space, about 2 cm. wide, in which pulsation, synchronous with the pulse beat, could be observed. The pulsation was plainly felt on palpation and could be recorded by a pneumographic transmitter. Pressure at this point was slightly painful.

A brown discoloration of the skin was noted as follows: on the neck; on the lower part of the sternum; over a wide area, of deep color, on the back from the neck to the level of the eighth dorsal vertebra, extending laterally over half the area of the scapulae. The margins of this area were notched, with a marbled appearance, and the pigmentation was most marked on the nape of the neck. Scattered over the hyperpigmented area on the back small spots of lighter color could be seen here and there (fig. 1).

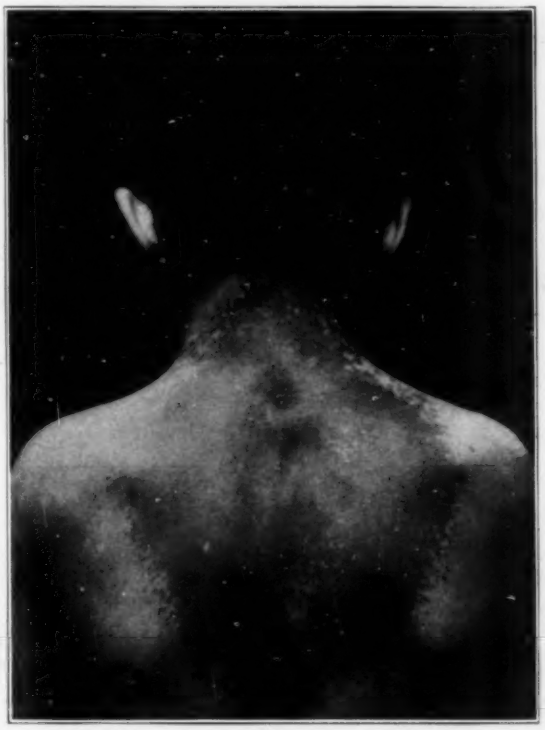

Fig. 1.—Area of pigmentation on the back.

Corresponding to the midpoint of the vertebral fissure, at the level of the sixth cervical vertebra, was a tuft of rather long hair, arranged in a whorl.

The terminal phalanges were missing from the second, third and fourth fingers of the left hand and from the first, second and third fingers of the right hand. The other fingers were stubby, and all except the first finger of the left hand were without a nail (fig. 2). On the fifth finger of the left hand a deep cicatrix was observed, which was not retracted, and there was pseudankylosis of the phalanx. On the palm of the left hand was an eschar, 2 cm. in diameter, the remains of a recent pustule. On both forearms there were a few small, white, circular cicatrices. The other parts of the upper extremities showed no special alterations in the skin.

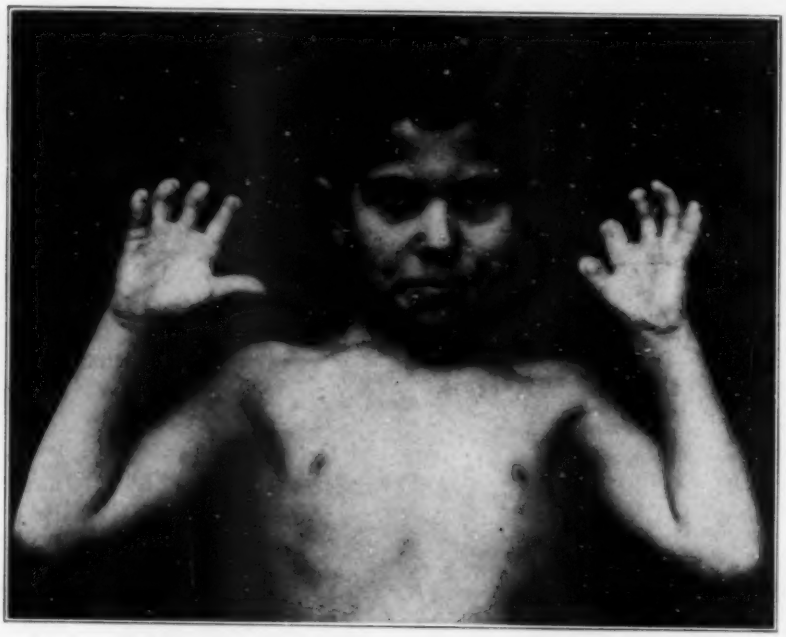

Fig. 2.—Deformities of the fingers produced by spontaneous amputations.

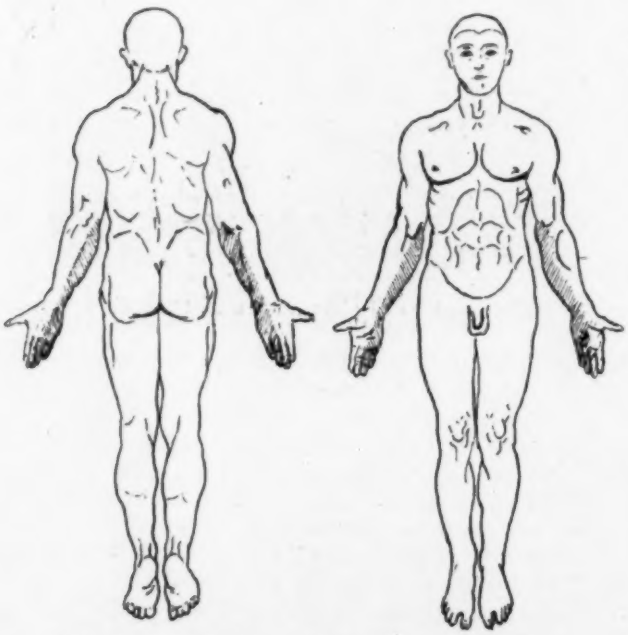

Fig. 3.—Distribution of the sensory disturbances.

Neurologic Examination.—The pupils were equal and of medium size, and reacted well to light and in convergence. The eye movements were normal. The nasolabial fold on the left side was slightly flatter than that on the right with the mouth closed or open. The protruded tongue deviated slightly toward the right, and was movable in all directions. The uvula was deviated to the left; it vibrated during phonation.

The neck movements were performed normally. The patient could raise himself from the supine to the sitting position without the aid of his arms.

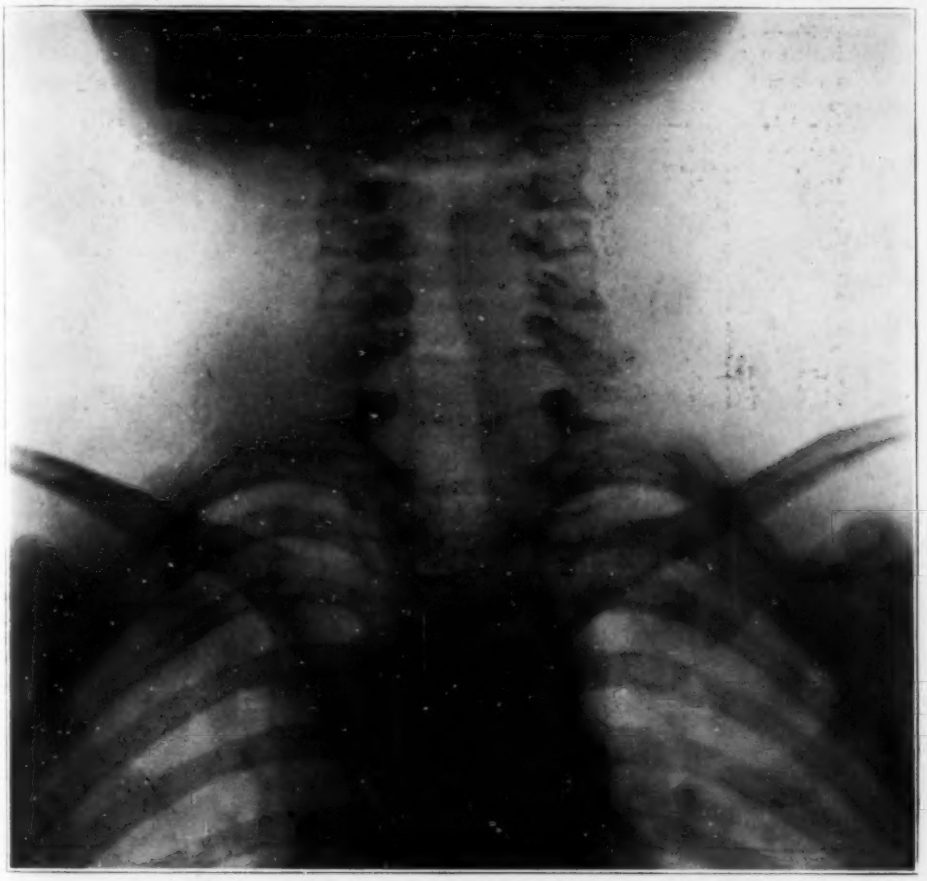

Fig. 4.—The vertebral defect.

Upper extremities: There was nothing of note in the posture. Muscular tone and trophism were normal. With the arms stretched forward there were no noticeable oscillations nor tendency to sag. The finger-nose test revealed no ataxy. Hand movements were limited by the amputations and ankyloses. All other movements of the fingers and forearm were normal on both sides.

Lower extremities: Nothing abnormal was noted in regard to posture. Muscular tone and trophism were normal. Muscular power was well conserved, and all movements, active and passive, were well performed. No ataxia was observed in the heel-knee test. There was no asynergia in the various move-

ments. The position in standing was normal; the Romberg sign was absent. There was no disturbance of gait.

Praxis: All commands were well and accurately carried out, and there was no adiadokokinesis. The test of "deviation of the index finger" gave normal results.

Reflexes: All tendon reflexes were present and equal on the two sides. The plantar responses were of flexor type, and other skin reflexes were prompt.

The oculocardiac reflex readings were 80-80. Skin stroking caused a normal red reaction over the whole surface of the body to a strong stimulus; the reaction was white to a weak stimulus.

Sensibility: To touch: Hypesthesia of radicular type involved the ulnar side of both forearms and hands, increasing from the elbow to the hand where there was complete anesthesia. The hypesthesia was more marked on the dorsal than

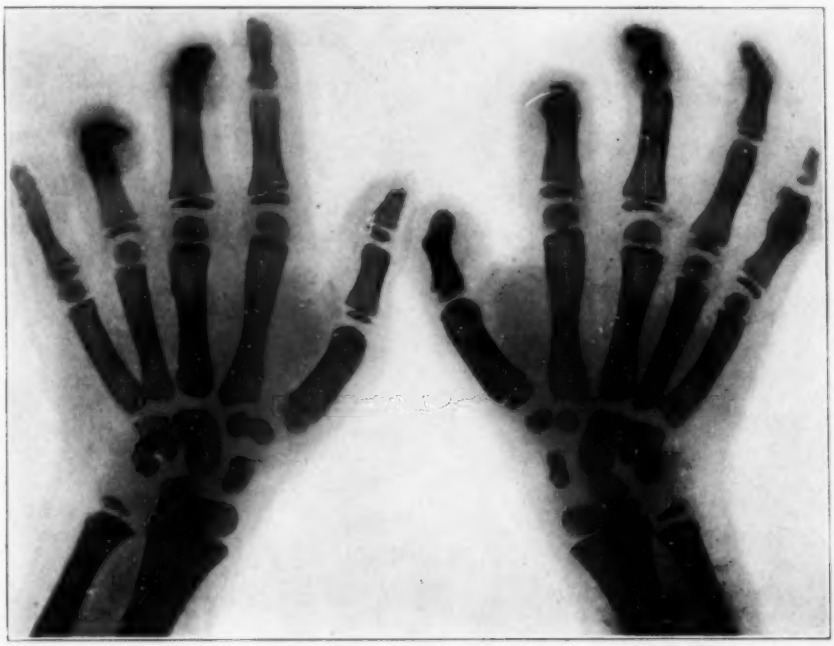

Fig. 5.—The bony deformities of the hands.

on the volar surface (fig. 3). To heat: Insensibility to heat and cold was present on the ulnar side of the forearms and the last two fingers; hypesthesia existed over all the remaining surface of the forearms and hands. To pain: Hypalgesia was present and was distributed like the hypesthesia to heat. Stereognosis: This was considerably diminished but not absent in the hands; on grasping objects the patient did not recognize the exact form, but was able to appreciate curves and angles. Bathyesthesia, normal. Pallesthesia, normal.

Organs of Sense.—Sight: Normal, both monocular and binocular; color vision normal; visual fields normal. Hearing: The speaking voice was heard well at 2 meters on each side, whispers at 1.50 m. Smell, normal. Taste, normal.

Internal Organs.—Physical examination revealed no anomaly of location or position of any organ.

Psychologic Test.—No disturbances were found of attention, perception or memory; the intelligence level was normal for the age of the patient.

Roentgenologic Examination.—The clinical findings in the cervical spine were confirmed: a wide cleft, with the vertebral bodies, the transverse apophyses and the intervertebral articulations all plainly visible. The laminae and spinous apophyses were not seen. The cleft decreased in width as it was prolonged downward to the fourth dorsal vertebra; it could be seen faintly through the shadow of the heart down to the fifth vertebra, where it ended (fig. 4).

The bones of the hands showed atrophy characterized by intense decalcification which increased from the proximal to the distal extremity. Nothing of importance was seen in the condition of ossification of the carpal bones, but in the metacarpal bones and phalanges there was moderate increase of the epiphyseal cartilages and irregularity of the line of ossification, which remotely suggested what is seen roentgenologically in rickets. In the carpal bones a marked thinning of the compact tissue was observed with a more than normal prominence of the spongy tissue, which had wide meshes. This was especially striking in the first metacarpal bone on both sides.

In the phalanges, ankylosis was present of the articulations between the second and third phalanges of the fourth and fifth fingers of the left hand, and the ungual phalanx was absent from these and the index finger. The distal extremity of the ungual phalanx of the thumb was missing. In the right hand, in addition to the findings already noted, there was total disappearance of the ungual phalanx of the thumb, and of the third phalanx of the second finger. In the third finger there was ankylosis between the second and third phalanges, with disappearance of the extremity of the third phalanx, which was considerably reduced in length and ankylosed to the distal extremity of the second, the latter being deformed and larger than normal. The third phalanx of the ring finger was sound. There was an increase in the interarticular space between the second and third phalanges of the fifth finger (fig. 5).

COMMENTS

The interest of the case described lies first in the unusual location of the lesion. Of all parts of the spine, the cervical region is that in which spina bifida is least frequently met. Moore, in 385 personal cases, found the cervical region involved in only 9 per cent; Pereis found it only three times in forty-four cases. Furthermore, among the various forms of spina bifida, the so-called "occult" form, according to the figures of Moore, of Clark [1] and of Bickner, represents only 5 per cent. Feil [2] regards superior cervical spina bifida occulta, of which the literature records only a few cases, as rather more frequent than is believed, and also as more frequent than median and inferior cervical spina bifida occulta. It often escapes notice because of other anomalies that deform or mask the primary lesions. Fuchs, on the other hand, has shown that there may be rudimentary forms of spina bifida discoverable only by means of roentgenography. The opening in the canal may, in fact,

1. Clark, S. N.: Report of a Case of Spina Bifida Occulta in the Cervical Region, J. Nerv. & Ment. Dis. **48**:201 (Sept.) 1918.

2. Feil: Progrès méd., 1920, p. 47.

present various degrees from a complete cleft with removal of the spinous apophyses to a simple incomplete vertical fissure.

But even more rare than the site are the cutaneous anomalies associated with the rhachischisis. As the photograph (fig. 1) shows, this patient had a tuft of hair arranged in a whorl at the center of the depression corresponding to the vertebral opening, at the level of the sixth cervical vertebra. While hypertrichosis of the vertebral region in cases of spina bifida is relatively frequent when the condition affects the lumbosacral region, it is extremely rare in the cervical and dorsal portions of the spine. Of forty-four cases that had been published up to 1903, as gathered by Garbini,[3] four affected the dorsal region, not one the cervical, and all others the lumbar and sacral regions; the hypertrichosis was always at the point corresponding to the cleft. In a large number of cases of spina bifida published later, I have found only one, that of Clark,[1] in which there was a tuft of hair arranged in a whorl at the spot corresponding to the space between the fourth and fifth cervical vertebrae, under which a small depression a few millimeters deep could be felt; here the symptomatology was limited to a slight hypokinesia of the fingers of the hands, without any disturbance of sensibility. Hence, the cervical region must be considered a most exceptional location for the presence of a tuft of whorled hair in the syndromes of spina bifida.

Quite as rare is the wide area of pigmentation on the back of my patient. There have been very few observations of this kind. Léri, Rabut and Queyrat [4] described a case of dorsolumbar spina bifida occulta with hyperpigmentation of the skin and leukomelanodermia, but here the arrangement was in zones and was unilateral. A case of cutaneous pigmented hemangioma in connection with a lumbosacral spina bifida occulta was reported by Rotgaus.[5]

On the other hand, it is not so rare to find the more deeply seated trophic lesions, of neuroparalytic nature, in the fields of innervation of the nerve trunks whose origin lies in the open vertebral segments—lesions which were present also in my case, in which, taken in connection with other nervous disturbances, they revealed the presence of anatomic lesions of certain segments of the spinal cord or of the corresponding nerve roots.

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3. Garbini: Tricosi lombo-sacrale e spina bifida occulta, Riv. di patol. nerv., September, 1903.

4. Léri, A., Rabut and Queyrat: Dermopatie à topographie unilateral avec pigmentation, leuco-mélanodermie, infiltration en ilots, etc. Spina bifida occulta, Bull. Soc. franç. de dermat. et syph., 1924, no. 4.

5. Rotgaus: Ein besonderer Fall von Spina bifida, Ztschr. f. d. ges. Neurol. u. Psychiat. **13**:223, 1919.

In my case the nervous disturbances consisted of the formation of pustules on the skin of the forearms and hands, and of disturbances of sensibility of syringomyelic type on both forearms from the elbow down, on the ulnar side of the forearms and on the hands, especially on the last two fingers. These hypesthetic zones correspond exactly to the area of projection of the sensory roots of the first dorsal, the eighth cervical and, in part, the seventh and sixth cervical segments. The fact that the anesthesia was limited to certain forms of superficial sensibility while the bathyesthesia, pallesthesia and the sense of position remained unimpaired and motility was normal, points to a lesion confined exclusively to the posterior cornua of the spinal cord segments, and, more precisely, along the posterior cornua after the point of separation of the fibers controlling superficial from those controlling deep sensibility. We know that the routes of sensibility to heat and to pain cross at the level of root entry, while some of the routes of tactile sensibility cross a little higher up and others join the routes of deep sensibility and ascend in the posterior columns of the same side without crossing until they reach the nuclei of the funiculi gracilis and cuneatus.

Various hypotheses have been put forward to explain the pathogenesis of the trophic disturbances associated with spina bifida. The old theory of Ornstein that the hypertrichosis is an atavistic survival, a reappearance of an organ that had philogenetically disappeared (whence the name "faun's tail" bestowed on it by Feré), has been discarded. Equally untenable is Virchow's theory that these disturbances are the result of an inflammatory process during the development of the spinal column. It is more probable, as Recklinghausen [6] suggested, that the hypertrichosis is the expression of a defect in embryonic development, a congenital malformation. As a matter of fact pathologic-anatomic examination of cases of spina bifida with dorsal hypertrichosis has not revealed lesions of inflammatory type, even in cases that have come to necropsy a few days after birth, while the presence of other teratologic malformations in connection with spina bifida is very common. In eleven cases collected by Garbini [3] in which the complete necropsy findings were reported, nine presented teratologic lesions; and monstrosities were found also in many cases of spina bifida reported by Recklinghausen, Virchow, Sutten, Muscatello, and others. In an accurate anatomic examination of seven cases of spina bifida that were also studied histologically, V. H. Keiller [7] found without exception developmental anomalies in various parts of the nervous system: hydromyelia, hydrocephalus, defects in the spinal ganglia and absence of differentiation in certain segments of the

6. Recklinghausen: Virchows Arch. f. Path. Anat., 1886.

7. Keiller, V. H.: A Contribution to the Anatomy of Spina Bifida, Brain **45**:31 (June) 1922.

spinal cord. Similarly, in a case of lumbosacral spina bifida described by Schwalbe and Grady, there were coincident anomalies in the cerebellum, pons, medulla oblongata and cervical cord.

It can hardly be doubted that the wide area of hyperpigmentation on the back in my patient had a similar origin. It is difficult to assume lesions of sympathetic innervation analogous to those described by Klippel and Weil,[8] by Nehl[9] and by De Lisi,[10] and studied in animals by Rynberk;[11] first, because the distribution of the pigmented area did not correspond with any area of projection of spinal or sympathetic nerves; secondly, because on the pigmented area of the back there was no other functional disturbance whatever of the sympathetic innervation, no difference in the manifestation of cutaneous sympathetic reflexes as compared with other parts of the skin such as could not have failed to be present in view of the intensity and great extent of the disturbance of pigmentation. On the other hand, the fact that the pigmented area was in precisely the same place as the spina bifida and the hypertrichosis supports the hypothesis that all these phenomena had a single teratologic origin.

Lastly, my case has one other important feature in the singular appearance of trophic and sensory disturbances of syringomyelic type. Sensory disturbances in spina bifida may take many different forms: hypesthesia to heat, to pain or to all kinds of stimuli; in some cases, disturbances of suggestive sensibility (neuralgia, Lange[12]); sometimes, a dissociation between superficial and deep sensibility. These cases are relatively rare. Klippel and Weil[8] regard their case, in which the first disturbances did not appear until the patient was 60 years of age, as the sole one in the literature up to 1921; a similar case was published a year ago by Cantaloube.[13] In such cases,[14] the association of a syringomyelic

8. Klippel, M., and Weil, M. P.: Syringomyélie et spina bifida combinés, etc., Presse méd., 1921, no. 98; Vitiligo metamérique, vitiligo commissural et naevus vitiligo, Rev. neurol. **36**:804 (Aug.) 1920.

9. Nehl: Ueber den Einfluss des Nervensystem auf den Pigmentgehalt der Haut, Ztschr. f. klin. Med. **81,** 1914.

10. De Lisi: Sulla topografia e sul significato di certe macchie brune della cute osservate in malati di mielite pottica lombare, Arch. gen. di neurol. psichiat. Psicoan. **2,** 1921.

11. v. Rynberk: Sulla metameria del sistema nervoso simpatico. L'innervazione pigmentomotoria, Arch. di fisiol., 1906, p. 601.

12. Lange: Nevralgies et contractures due à une spina bifida occulta des vertèbres cervicales, Bull. Soc. de pédiat. de Paris, 1921, no. 2.

13. Cantaloube, P., and Picheral, C.: Syndrome syringomyélique congénitale et spina bifida occulta cervico-dorsal, Rev. neurol. **1**:308 (March) 1924.

14. The association of these two disease symptoms is as a rule incompatible with life; nearly all examples of spina bifida and true syringomyelia have been found in fetuses or in infants that died shortly after birth (cases reported by Redlich, Leyden, Schwalbe, Wichtig and others).

syndrome with more or less numerous signs of embryonic developmental defects throws some light on the pathogenesis of congenital syringomyelia. It certainly points rather to a teratologic origin of these two conditions than to an inflammatory (Achard, Joffroi) or neoplastic (Dejerine, Schwalbe) origin, and this is further borne out by the negative histologic findings in the case of Klippel and Weil. These two authors assume a single cause for spina bifida and syringomyelia in their case: hydromyelia, which produced simultaneous lesions of spinal cord and column. Hence, according to these authors, the pathogenesis of the affection lies in a congenital hypertension of the cerebrospinal fluid. From this they propose to individualize the syndrome spina bifida plus syringomyelia under the name "hydromyelic, ependymal and arachnoid syndrome."

But the fact that in these cases the first symptoms of syringomyelia appeared after birth, sometimes many years after it (in the case of Klippel and Weil sixty years), points to the conclusion that, while congenital malformations may of themselves be sufficient directly to produce syringomyelic syndromes (especially trophic disturbances), in most cases they do no more than give a predisposition to true syringomyelia, and that actually to produce this, other causes, inflammatory or neoplastic, must be superadded. Such a cause might lie in a very fine gliomatosis that escapes recognition on a histologic examination that has not plumbed the entire cerebrospinal axis for the whole length of the syringomyelic cavity.

This hypothesis would account for the late beginning of syringomyelic disturbances in cases in which from birth there undoubtedly existed alterations of development (cases of Léri,[15] Marie [16] and Klippel and Weil).

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15. Léri, A.: Spina bifida occulta cervical, Bull. et mém. Soc. méd. d. hôp. de Paris **47**:509 (March 23) 1923. Léri, A., and Lamy: Vitiligo zoniforme; sclerodermie; spina bifida, Bull. Soc. franç. de dermat. et syph., 1923.

16. Léri, A., and Marie, P.: Spina bifida occulta cervical révélé exclusivement par une quadriplégie à début extrêment tardif, Bull. et mém. Soc. méd. d. hôp. de Paris **46**:1138 (July 21) 1922.

FURTHER STUDIES ON THE ETIOLOGY OF EPIDEMIC HICCUP (SINGULTUS) AND ITS RELATION TO ENCEPHALITIS *

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Epidemic hiccup, while usually considered lightly, is by no means always a trivial affliction. Patients having severe spasms for more than two days often suffer from physical exhaustion and weakness, out of proportion to the mild constitutional symptoms. Attacks of varying severity may last for weeks and even months. Fatal cases have been reported.[1] Fortunately, however, the disastrous residuals of encephalitis apparently do not develop, although hiccup and other myoclonic spasms are not uncommon in cases of epidemic encephalitis.[2] Sicard considers epidemic hiccup as a para-encephalitis.[3] Since the pandemic of influenza in 1918, epidemics of hiccup have usually occurred in association with epidemics of encephalitis throughout most of the civilized world. Aronowicz [4] describes an epidemic of hiccup which occurred just preceding and during the early part of an epidemic of encephalitis in Petrograd in 1923. He mentions the reports of similar epidemics in different parts of Russia, Germany, the Netherlands and Italy. Lhermitte [5] also calls attention to the close relationship of spasmodic hiccup to encephalitis. Belloni [6] and Buffone [7] describe similar epidemics of hiccup occurring during an outbreak of mild influenza. Boyd [8] reports an extensive epidemic of hiccup which occurred during the epidemic of encephalitis in Winnipeg in 1919, and a milder outbreak

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1. Nelken, L.: Ueber gehäuftes Vorkommen von schwerem Singultus, Med. Klin. **20**:1505-1506 (Oct. 26) 1924.

2. Brain, W. R.: Epidemic Hiccup and Encephalitis Lethargica, Brit. M. J. **2**: 856-857 (Nov. 10) 1923.

3. Sicard, J. A.: Epidemic Hiccup. Para-Encephalitis, Médicine, **5**:341-342 (Feb.) 1924.

4. Aronowicz, G. D.: Eine Singultusepidemie in Petersburg, Klin. Wchnschr. **2**:1648-1649 (Aug. 27) 1923.

5. Lhermitte, J.: Le hoquet épidémique; forme singultueuse de l'encéphalite épidémique, Presse méd. **28**:916-919 (Dec. 18) 1920.

6. Belloni, G.: Complicanze e postumi rari dell' influenza, Riforma med. **39**: 198-201 (Feb. 26) 1923.

7. Buffone, F.: Il singhiozzo epidemico equivalente dell' influenza, Policlinico (sez. prat.) **29**:682-683 (May 22) 1922.

8. Boyd, W.: Epidemic Encephalitis: the Second Winnipeg Outbreak, Quart. J. Med. **18**:153-173 (Jan.) 1925.

in 1923, during a second epidemic of encephalitis. He suggests that the reason only a few patients with hiccup developed outspoken attacks of encephalitis may have been that the hiccup produced immunization against encephalitic manifestations of the disease. Cadham's [9] findings in a third epidemic in Winnipeg in November, 1924, support this view, for no case of encephalitis occurred in which there had been a previous attack of hiccup. During the third epidemic of hiccup in Winnipeg, reported by Cadham, as in the one I studied, the spasms were usually not so severe, the quiescent intervals were longer, the total duration of the attack was shorter than in previous epidemics, and exhaustion following the attack was less common. Outspoken cases of encephalitis were relatively rare in 1924, but instead there occurred cases of hyperesthesia of the scalp, face and neck, and as the epidemic of hiccup disappeared and "influenzal" infection of the respiratory tract became more marked, nausea and vomiting, and varying degrees of neuritis, radiculitis, myelitis and encephalitis, or of combinations of these, appeared.

In families or other groups, one person may have encephalitis and another only prolonged hiccup, or the same person may become lethargic and have hiccup. Prolonged contact with patients having hiccup has resulted in contraction of encephalitis, and vice versa.[10]

In previous publications I have reported the isolation of a streptococcus in cases of epidemic hiccup with which spasms of the diaphragm, often associated with hiccup, have been produced experimentally in animals.[11] This syndrome was produced with suspensions of nasopharyngeal swabbings containing the streptococcus, with freshly isolated pure cultures and after many rapidly made subcultures, with filtrates of active cultures and with suspensions of the dead bacteria.[12]

The animals that succumbed to prolonged attacks of hiccup manifested, as do patients with fatal attacks, outspoken signs of encephalitis. Moreover, through artificial cultivation or successive passage through animals, it repeatedly happened that the streptococcus of hiccup lost the power of producing spasms of the diaphragm and other muscles, and instead produced lethargic and other forms of encephalitis. I have isolated a similar streptococcus in different forms of epidemic encepha-

9. Cadham, F. T.: Hiccup: the Winnipeg Epidemics, J. A. M. A. **84**:580-582 (Feb. 21) 1925.

10. Netter, A.: Origine commune due hoquet épidémique et de l'encéphalite léthargique; relations chronologiques, Bull. et mém. Soc. méd. d. hôp. de Paris **45**:46-48 (Jan. 21) 1921.

11. Rosenow, E. C.: Diaphragmatic Spasms in Animals Produced with a Streptococcus from Epidemic Hiccup, J. A. M. A. **76**:1745-1747 (June 18) 1921.

12. Rosenow, E. C.: The Production of Spasms of the Diaphragm in Animals by Living Cultures, Filtrates, and the Dead Streptococci from Epidemic Hiccup, J. Infec. Dis. **32**:72-94 (Jan.) 1923.

litis and have produced the symptoms and lesions in animals, findings that have since been corroborated by Dr. Evans of the Hygiene Laboratory. In still another study, marked changes in the virulence and the disease-producing power of the streptococcus from encephalitis have been induced experimentally. In one case of encephalitis in which there was a history of influenza, various forms of encephalitis, including that manifested by spasms of the diaphragm and other muscles, were produced in animals on intracerebral inoculation of the streptococcus isolated. It then had little or no effect on intratracheal injection. After being rendered highly virulent by rapid passage through animals, it produced suppurative meningitis on intracerebral inoculation, and on intratracheal injection, varying degrees of hemorrhagic edema of the

TABLE 1.—*Percentage Incidence of Symptoms in Animals Following Inoculation of Streptococci from Epidemic Hiccup, from Poliomyelitis and from Normal Controls*

Source	Cases	Animals Injected	Symptoms, per Cent: Muscular Spasms: Diaphragm	Abdominal	Other	Total	Abnormal Movements and Postures: Nystagmus	Tic-like Movements	Ataxia	Turning of Head	Tremor	Hyperpnea	Paralysis	Lethargy
Epidemic hiccup:														
First series (reported)	8	96	42	17	50	74	22	11	38	19	53	45	29	22
Second series	8	30	37	20	70	87	3	3	30	3	67	57	20	7
Third series	12	50	48	46	76	80	3	3	14	10	52	24	40	5
Total	28	176	42	25	59	76	14	7	29	14	55	40	30	15
Poliomyelitis:														
Acute cases	38	58	3	2	7	7	2	3	21	9	14	14	78	3
Contacts	35	25	0	0	4	4	4	4	64	4	28	20	72	4
Controls	75	57	2	2	2	2	0	2	9	2	7	0	12	0

lung, bronchopneumonia and leukopenia. Both types of strains lost all virulence after cultivation for one year. In these and similar results, an experimental basis for the relationships believed to exist in cases of influenza, epidemic hiccup and encephalitis appeared to be demonstrated, for the same streptococcus produced symptoms and lesions of these widely different diseases, depending on whether it was in the highly virulent or pneumotropic phase, when influenzal infection of the lung occurred, or in the less virulent but neurotropic phase, when polioencephalitis and allied conditions were prone to develop.

I shall report here further results in two additional outbreaks of epidemic hiccup and experiments which bear on the mechanism of the production of the spasms of the diaphragm by the streptococcus of epidemic hiccup, the relation between epidemic hiccup and epidemic encepha-

litis, and the specific treatment of hiccup. The technic used was similar to that described in my previous studies.[13]

CLINICAL FINDINGS AND ANIMAL EXPERIMENTS

The first of the two additional groups to be reported consisted of eight cases in which attacks were prolonged (table 1, second series). Five of these cases occurred between Oct. 4, 1922, and April 17, 1923, and three between Jan. 22 and May 14, 1924. The second group, comprising twelve cases (table 1, third series), occurred between Nov. 17 and Dec. 9, 1924. In none of the eight cases in the first group were accompanying symptoms noteworthy. The attack lasted two days in one case, three days in two cases, seven days in three, and ten days in two. All of the persons were well otherwise. Two of the twelve in the second group were nauseated and vomited before hiccup began, and two developed neuritic pains, one of the forehead, the other of the left side of the scalp and ear, as spasms of the diaphragm disappeared. The neuritic pain lasted for several days and then disappeared without further manifestations. One patient developed moderate lethargy after the hiccup disappeared, and one had transient diplopia during the attack. The paroxysms of spasms in the cases of the second group were less severe, the quiescent intervals longer, and the average duration of the disease shorter, than in those of the first group. In one case (case 4) generalized myoclonic encephalitis, instead of spasms of the diaphragm, was manifested, but the case is included in this series because the attack occurred at the time hiccup was epidemic in the community and because the animal experiments serve as good controls. All of the cases occurred in men. The ages ranged from 21 to 54 years. Mild symptoms of nasopharyngitis and hyperemia of the throat were present in most of the cases. The pulse and temperature were usually normal. The respirations between the paroxysms, while seemingly normal, varied greatly in amplitude and rate. Cultures of nasopharyngeal swabbings on blood agar often differed little from similar cultures from normal throats, although usually a large number of green-producing streptococci were found. This difference was particularly striking in the spreads made in cases at the time of the attack and after recovery. Precipitin tests of the cleared nasopharyngeal swabbings with the polioencephalitis-antistreptococcus serum and other hyperimmune horse serums were positive in six of ten cases at the time of the attack, and negative in all of five cases from two to four weeks after recovery. The reaction was negative in all of the control serums. The streptococcus from positively affected animals in each of eight cases was agglutinated specifically in the

13. Rosenow, E. C.: The Production of Spasms of the Diaphragm in Animals with a Streptococcus from Epidemic Hiccup, J. Infec. Dis. **32**:41-71 (Jan.) 1923; footnote 12.

poliomyelitis and encephalitis serums, while only three of nine strains of green-producing streptococci isolated from the brains of rabbits injected with material from normal persons were so agglutinated (table 2).

The serum from four patients, obtained from one to three weeks after recovery, agglutinated specifically four of seven hiccup strains. The serum obtained during the attack in one case of prolonged hiccup (case 3) was found not to have the power to neutralize poliomyelitis virus, whereas that obtained nineteen days later neutralized it completely. The monkey injected with the serum-treated virus remained well and succumbed later to injection of the virus alone. On the other hand, the serum from the boy with myoclonic encephalitis (case 4), whose symptoms subsided so promptly after serum treatment, had no

TABLE 2.—*Mortality and Results of Cultures in Animals Injected with Streptococci from Epidemic Hiccup, from Poliomyelitis and from Normal Controls*

		Animals					
			Died			Green-Producing Streptococcus in	
Source	Cases	Injected	Number	Per Cent	Cultured	Brain, per Cent	Blood per Cent
Epidemic hiccup:							
First series (reported)	8	96	67	70	81	94	38
Second series	8	30	22	73	18	78	22
Third series	12	50	34	68	31	84	30
Total	28	176	123	70	130	89	37
Poliomyelitis:							
Acute cases	23	58	47	81	49	90	35
Contacts	35	25	21	84	23	91	52
Controls	15	37	16	28	29	31	27

neutralizing power over virus during, or following, the attack. Spasms of the diaphragm or other muscles were produced in one or more animals in each of the twenty cases studied. The incidence of symptoms in the animals injected with the streptococcus from epidemic hiccup and, by contrast, in animals injected with the streptococcus from poliomyelitis and poliomyelitis contacts, and in those injected with material obtained from the throats of normal persons as controls, are summarized in table 1.

In general, the incidence of muscular spasms and other symptoms in the animals injected corresponds closely in the three series of cases of epidemic hiccup. In the total of twenty-eight cases studied, 176 animals were inoculated. Of these, 42 per cent were seen to have spasms of the diaphragm, 25 per cent spasms of the abdominal muscles and 59 per cent spasms of other muscles; 76 per cent had spasms of one or more muscle groups. Tremors of muscles and hyperpnea, the most common accompanying findings, occurred in 55 per cent and 40 per cent, respectively, while definite outspoken weakness or paralysis occurred in 30 per cent

and lethargy in 15 per cent. These findings are in sharp contrast to those following the injection of the streptococcus from poliomyelitis and poliomyelitis contacts. Here, spasms of the diaphragm did not exceed 3 per cent, and spasms of the muscles 7 per cent. The incidence of tremor and hyperpnea and lethargy was also much lower. The incidence of flaccid paralysis, on the other hand, was much higher, 78 per cent and 72 per cent, respectively, in the two groups. The findings in hiccup and poliomyelitis and poliomyelitis contacts are in turn different than those noted in fifty-seven animals injected with material from the throats of seventy-five normal controls. Here the highest incidence of muscular spasms was 2 per cent, of tremors 7 per cent and of paralysis 12 per cent. Marked hyperpnea and lethargy were not observed.

Striking as these figures are, they do not adequately express the marked specificity of the different hiccup strains. The number of animals that developed spasms of the diaphragm in the hiccup group was undoubtedly higher than the figures indicate, for the spasms were sometimes mild and transient, and the animals were not observed, as a rule, during the night. The myoclonic spasms were often more pronounced in the animals injected with the streptococcus from the more severe cases, and sometimes corresponded in type to those noted in the original case. The animals injected with the streptococcus from the patient with myoclonic spasms (case 4), especially of the masseters, but without spasms of the diaphragm, developed extreme rigidity and spasms of the masseters and twitchings of the muscles of the neck and shoulders, but no spasms of the diaphragm. Moreover, similar injections in animals of suspensions of nasopharyngeal swabbings from persons having persistant hiccup due to other conditions, such as laparotomy, cerebellar tumor and aneurysm of the aorta, failed to produce spasm of the diaphragm in a single instance. In a similar study of cases of neuritis with or without myelitis that occurred during and after the epidemic of hiccup, only three of twenty-one rabbits injected developed spasms of the diaphragm. Two of these were injected with the streptococcus from two patients who had transient hiccup and one with the streptococcus from a patient who lived in a house in which a case of persistent hiccup had occurred ten days before, and who developed nausea, vomiting and neuritic pains. Evidence of specificity, often extreme, was revealed in the findings at necropsy. Thus, of seventy-three rabbits injected intracerebrally with material from twenty-one cases of epidemic hiccup in which search for lesions of peripheral nerves and cord was made, only two (9.5 per cent) revealed gross hemorrhages of peripheral nerves, four of the nerve roots and six of the spinal cord; whereas in the neuritic group, eight of twenty-one rabbits (38 per cent) revealed lesions of peripheral nerves, and only one of sixteen injected with material from the patients who had no accompanying symptoms of myelitis had hemor-

rhages in the cord, while nine of twenty-one (43 per cent) injected with material from patients who had symptoms of myelitis had gross hemorrhages of the cord.

The mortality rate was practically the same in the three series of experiments in cases of epidemic hiccup, being respectively 70, 73 and 68 per cent, or an average of 70 per cent (table 2). The death rate in cases of poliomyelitis and poliomyelitis contacts was somewhat higher, 81 and 84 per cent, while that in the control series was only 28 per cent. The incidence of the isolation of green-producing streptococci from the brain and blood in the three series corresponded closely to the mortality rate, and may be regarded as expressing the neurotropism of this group of organisms compared with others as found in the throat. Thus, in the epidemic hiccup series, it was isolated from the brain in 89 per cent of the animals and from the blood in 37 per cent; in the poliomyelitis series in 90 and 35 per cent; in the poliomyelitis contacts in 91 and 52 per cent, while in the control series in only 31 and 27 per cent, respectively.

As a further check on the results obtained in cases of epidemic hiccup, animals were injected in the usual manner with nasopharyngeal swabbings from six patients with epidemic hiccup from two to four weeks after recovery. In none of the twelve rabbits injected did spasms of the diaphragm appear; in only one were slight tremor and twitchings of the masseters evident; in three abnormal movements of the head appeared, resembling spasmodic torticollis; none died. The gross and microscopic lesions in the animals in this series were similar in every respect to those found in my previous studies.[14]

IMMUNIZATION EXPERIMENTS

The moderate immunity of animals that have recovered from hiccup following the inoculation of the living streptococcus, and the dead bacteria and filtrates, was reported in a previous paper.[12] The chief difficulty in experiments in immunization lies in the fact that the strains tend to lose their specific infecting power during the periods of immunization, especially on aerobic cultivation. A vaccine prepared from the streptococcus preserved in dense suspensions of glycerin and sodium chloride solution was used on the basis of the previous finding, and with what appeared to be beneficial effects in four cases of refractory hiccup.

In order to overcome so far as possible the difficulty in immunization, pure cultures of strains freshly isolated from the brain and cord of

14. Rosenow, E. C.: Changes in Streptococcus from Encephalitis, Induced Experimentally, and Their Significance in the Pathogenesis of Epidemic Encephalitis and Influenza, J. Infec. Dis. **33**:531-556 (Dec.) 1923; Streptococci in Relation to the Etiology of Epidemic Encephalitis, ibid. **34**:329-389 (April) 1924.

positively affected animals were inoculated into tall columns of meat infusion contained in tubes sealed with a screw cap containing a rubber disk. These were incubated for twenty-four hours and then kept at room temperature in the dark as stock strains. Subcultures from these were made in dextrose broth for the test injections. Preservation of individual strains in the meat infusion ranged from fourteen to thirty-four days before the immunizing antigen was prepared, and from forty-four to sixty-five days before the subculture in glucose brain broth was made for the test injection. The eighteen-hour growth in the glucose broth, representing equal parts of six strains, was suspended in glycerin, two parts, and 25 per cent solution of sodium chloride, one part, so that 1 cc. represented the growth from 150 cc. of broth. Specific agglutinating and precipitating properties of streptococci have been maintained in this way for a long time. The antigen for immunization was prepared from this dense suspension in glycerin and sodium chloride solution. Twelve rabbits, weighing from 1,600 to 2,000 Gm., were immunized by intravenous injection over a period of four weeks. During the first week three daily injections were given of 1, 1.5 and 2 cc. each of the heat-killed suspension in a solution of sodium chloride containing 2,000,000,000 organisms in each cubic centimeter; during the second week, the equivalent unheated suspension in like dosage; during the third week the equivalent unheated suspension in doses of 2.5, 3.0 and 3.5 cc., and during the fourth week, equivalent amounts of the unheated suspension treated with an equal amount of 1 per cent solution of sodium ricinoleate, according to the method of W. P. Larson of the University of Minnesota. The animals remained well, and 10 cc. of blood was withdrawn from the heart seven days after the last injection. The serum of each of these immunized rabbits was found to have developed moderate agglutinating power over suspensions, and precipitating power over clear extracts of suspensions of the strains injected, as well as over five other hiccup strains. The test injection, consisting of a mixture of equal parts of eighteen-hour cultures in glucose brain broth of four of the strains used for immunization, was given eight days after the last immunizing injection, six normal controls being used. One half of each group received 0.2 cc., intracerebrally, of the glucose-brain-broth cultures diluted with an equal amount of gelatin Locke solution; the other half, 0.2 cc. of a 1:100 dilution. All of the six control animals died: two within a day, three within two days and one within three days after injection. Three developed marked myoclonic spasms of muscles including the diaphragm; two, slight spasms and tremors, and one, no tremors or spasms. The last three showed marked hyperpnea and weakness soon after injection; the first three showed weakness after muscular spasms had continued for many hours. Two additional normal rabbits injected with a 1:1,000 and 1:10,000 dilution remained perma-

nently free from symptoms. Of the twelve immunized rabbits, only four died (33.33 per cent), one within two days and three within three days. Five manifested marked myoclonic spasms of muscles including the diaphragm, and four, mild twitchings or tremors, while three remained free from symptoms. Two of the four that died showed no tremors or spasms but marked weakness instead and markedly increased respirations. In one this was associated with lethargy. Only one died with a typical picture of generalized myoclonic encephalitis. The cultures of pipettings from brain and cord of those that died in both groups yielded large numbers of the streptococcus.

SERUM TREATMENT

The encephalitis immune serum was used in the treatment of six patients with hiccup and one with encephalitis associated with spasms of the diaphragm; and the poliomyelitis immune serum, also having marked agglutinating power over the streptococcus, was used in the treatment of one patient with myoclonic encephalitis. Injections of from 10 to 20 cc. were given intramuscularly or intravenously twice daily. The results were similar to those noted in cases 4, 5 and 7. Spasms of the diaphragm or other muscles either disappeared entirely or became less marked and less frequent after the first injection, and disappeared entirely after the second. The encephalitis-antistreptococcus serum was used in the treatment of a total of nine rabbits that had developed marked spasms of the diaphragm following injection of the streptococcus from five patients with epidemic hiccup. The dosage and results in all were similar to those recorded in the rabbits injected with the streptococcus from cases 1, 2 and 4. The spasms disappeared in all; seven rabbits recovered completely and two died, one from respiratory failure due to infection by the streptococcus, the other from accidental infection due to *Bacillus bronchisepticus*. The effect of normal horse serum was tested in three parallel experiments. Spasms were not relieved in any of these but continued until death. All of six untreated control rabbits also died.

ILLUSTRATIVE CASES

CASE 1.—A physician, aged 32, on the afternoon of Nov. 10, 1924, from no apparent cause, began to have persistent attacks of hiccup with remissions at irregular intervals. Holding of his breath and the drinking of water gave no relief. He slept well the first night but on arising the next morning, the hiccup returned. During the second day, the attacks were, for the most part, of two hours' duration with intermissions lasting about two hours. The spasms of the diaphragm with hiccup occurred from one to four times a minute and varied greatly in intensity. On the evening of the second day, hiccup did not disappear until after the administration of ⅛ grain (0.008 Gm.) of morphine hypodermically. The patient then slept all night. During the third day he had four or five attacks which seemed to be aborted by the drinking of water. On the fourth day

two slight attacks occurred. The day after hiccup disappeared he suffered from mild photophobia and a dull pain associated with marked tenderness of the skin over the forehead and upper part of the face. This lasted for several days and then disappeared. Examination, November 12, revealed moderate hyperemia of the nasopharynx and tonsils. A small amount of pus was expressed from the tonsils. The teeth were normal. There was no fever, his general health was good and the pulse was normal. The respirations during quiescent intervals appeared normal on superficial examination, but on close observation distinct irregularity in rate and amplitude was noted.

Two animals were injected directly, November 12, one with material swabbed from the nasopharynx and the other with the pus expressed from the tonsil, each suspended in 2 cc. of gelatin Locke solution. Persistent spasms of the diaphragm associated with synchronous spasms of abdominal muscles developed in both ani-

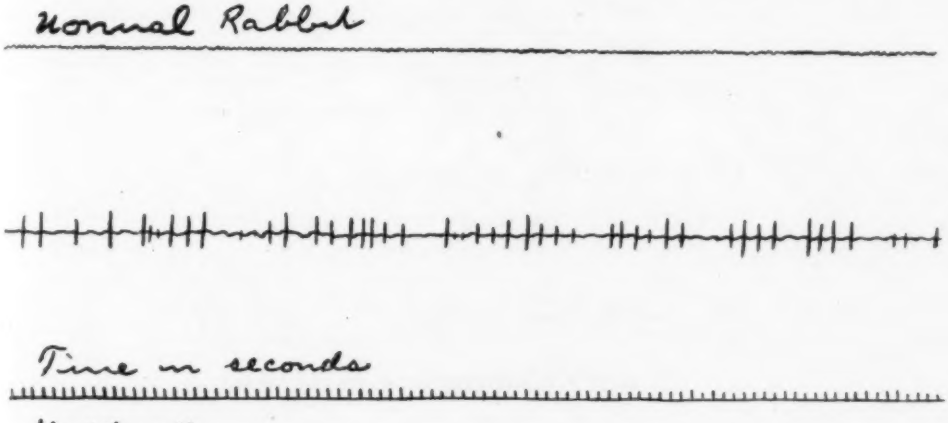

Fig. 1 (rabbit 548).—Intracerebral injection Nov. 12, 1924, with 0.2 cc. of the nasopharyngeal swabbings, case 1. The rhythmic spasms of the diaphragm and abdominal muscles indicated by the vertical lines may be noted.

mals (fig. 1). The spasms of the abdominal muscles, especially along the costal margin, were easily detected on palpation and these, with the synchronous spasms of the diaphragm, could be seen with the fluoroscope. The green-producing streptococcus in the primary culture in glucose brain broth from the brain of this rabbit was injected into two rabbits, one receiving 0.2 cc. of a 1:100 dilution, the other 0.2 cc. of a 1:1,000 dilution in gelatin Locke solution. Both manifested marked symptoms of myoclonic encephalitis and marked paralysis, to which they succumbed, one in two days, the other in three days. The nose of one monkey (*Macaccus rhesus*) was packed with gauze soaked in the same culture. Two days later the pack was removed; after tremor and trembling of fingers and forearm, increased respiration and spasm of the diaphragm had appeared. These symptoms continued for one day after the removal of the pack and then disappeared.

A single colony was fished from the blood-agar plate inoculated twelve hours previously with pipettings from the brain of one of the rabbits that developed hiccup (fig. 1). This was inoculated into warmed glucose-brain broth. The resulting culture was then transferred rapidly through ten subcultures, when three rabbits and four guinea-pigs were injected intracerebrally. The amount injected ranged from 0.1 cc. of the undiluted culture to 0.2 cc. diluted 1:100. The three rabbits and three of the four guinea-pigs manifested muscular spasms, including spasms of the diaphragm (fig. 2). One of the rabbits was given the encephalitis immune serum after marked spasms and weakness had developed. Three injections of 5 cc. each were given at intervals of six and twelve hours. The spasms disappeared and muscular strength returned synchronously, and the animal recovered. The two untreated rabbits died. The filtrate of the tenth subculture of the streptococcus in glucose-brain broth was injected intracerebrally into one rabbit (2 cc.) and into one guinea-pig (1 cc.). The rabbit showed tremor and twitching of the masseters several hours after injection; this had disappeared

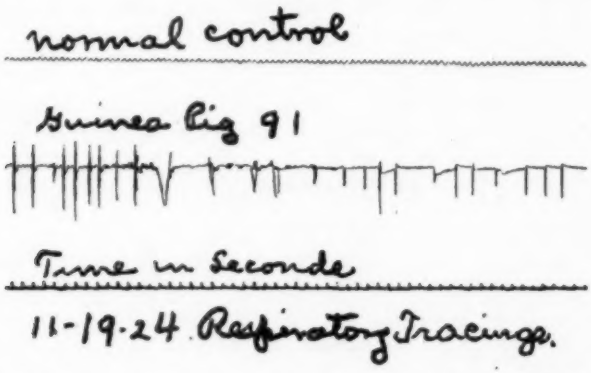

Fig. 2 (guinea-pig 91).—Intracerebral injection Nov. 18, 1924, with 0.2 cc. of a 1:100 dilution of glucose brain-broth culture of the streptococcus in the tenth subculture and after one animal passage, case 1. The irregularly timed spasms of the diaphragm may be noted.

by the following morning. Two days later it showed moderate lethargy and increased muscular tonus, especially of the ears, jaw and neck, which lasted for a week and then disappeared. The guinea-pig remained free from symptoms. The organisms from the tenth subculture in glucose brain broth were centrifugalized, washed once in solution of sodium chloride, suspended in an equivalent amount of the solution and killed by heating to 56 C. for one hour. Control cultures remained sterile. These were then injected intracerebrally into one rabbit, two guinea-pigs and two monkeys, 1.5, 0.5 and 3.0 cc. of the suspension, respectively, being given. All developed tremor and twitchings of muscles and spasms of the diaphragm. The spasms began two and one-half hours after the injection into the rabbit, five hours after the injection into the guinea-pigs and in six hours after injection into the monkeys. The spasms were most marked in the guinea-pigs (fig. 3). The monkeys recovered; the guinea-pigs and rabbit succumbed. Cultures of brain and cord, spinal fluid and blood remained sterile. Smears from the edema fluid surrounding cervical nerve roots and the anterior aspect of the medulla revealed leukocytes, round cells and many diplococci within and without leukocytes in various stages of disintegration. Two rabbits were injected with cultures of the

swabbings obtained from the nasopharynx and tonsils December 8, twenty-five days after recovery. Both remained well and free from symptoms.

Comment.—The points of special interest in this case are the unusually high incidence of spasms of the diaphragm and other muscles (seventeen of nineteen animals) produced with the living freshly isolated streptococcus, and in the tenth culture generation with the living and heat-killed organisms and the corresponding filtrate; the positive result

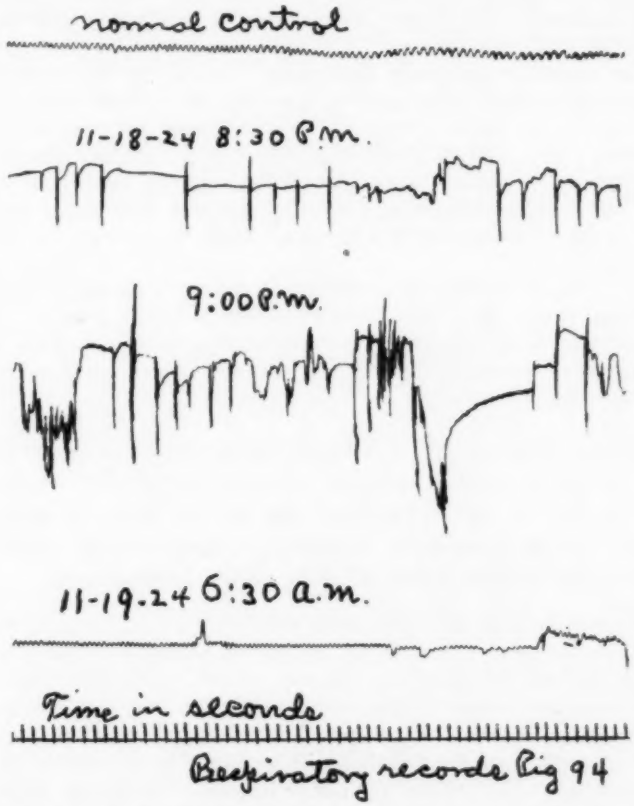

Fig. 3 (guinea-pig 94).—Intracerebral injection Nov. 18, 1924, at 3:30 p. m., with 0.6 cc. of the washed heat-killed streptococcus from the tenth subculture, case 1. The irregularly timed spasms of the diaphragm at 8:30 and 9 p. m. and approximately normal respiration the following morning may be noted.

in the monkey after packing the nose with gauze soaked in the culture; the negative results with swabbings from the throat after recovery; the late development of lethargy in the rabbit injected with the filtrate of the streptococcus in the tenth subculture, and the cessation of spasms of the diaphragm with recovery of the rabbit treated with the encephalitis-antistreptococcus horse serum.

Case 2.—A man, aged 26, from no apparent cause, began to hiccup Nov. 14, 1924. The associated spasms of the diaphragm varied in intensity but were never violent, occurring from one to ten times a minute for as long as two hours during the day, disappearing at night. The attacks were followed by quiescent intervals of about the duration of the preceding spell of hiccup; they lasted three days and then disappeared. The patient's general health was good; the feeling of slight distress along the costal arch during the spasm was the only symptom. Examination was negative except for moderate congestion of the throat and pus in the tonsils.

Suspensions of nasopharyngeal swabbings and pus expressed from tonsils, obtained November 15 and 17, were injected intracerebrally into three rabbits and two guinea-pigs in the usual manner. The three rabbits and one of the guinea-pigs had muscular spasms including the diaphragm. Two of the rabbits were treated with two injections of 5 cc. each of my encephalitis immune horse serum, and one with normal horse serum. Spasms of the diaphragm and other muscles disappeared promptly and did not recur (fig. 4). Spasms in the animal receiving normal horse serum continued unabated until death, twelve hours after the serum was given. Both of the animals became very weak, and respirations were embarrassed before the serum treatment was begun; death ensued two days later from respiratory paralysis.

Two rabbits were injected intracerebrally in the usual manner with swabbings obtained three weeks after the patient's recovery. Both remained free from twitchings or spasms of muscles. One manifested transient weakness, and later, ticlike movements of the head; the other remained free from acute symptoms, but later the ticlike movements of the head appeared.

Comment.—The findings of special interest in this case are the relief from spasms in the rabbits injected with the encephalitis serum, which was not the case in the rabbit receiving normal horse serum, and the absence of muscular spasms in the animals injected with material from the patient's throat three weeks after recovery from hiccup.

Case 3.—A man, aged 66, registered at the Mayo Clinic, Nov. 14, 1924, seeking relief from hiccup, which had been almost continuous for four days. Four years before, he had had a similar attack of hiccup lasting four days. By the use of sedatives and antispasmodics, the spasms were reduced in severity and prevented for several hours at a time, permitting sleep. They disappeared entirely after the nasopharynx had been washed with sodium chloride solution on November 17. December 9, he returned for advice because of unnatural sleepiness; he would repeatedly fall asleep during the day, despite the fact that he slept from eleven to twelve hours at night. This disappeared after about a week. Examination revealed moderate arteriosclerosis. The systolic blood pressure was 160, the diastolic 90. The leukocytes numbered 7,400 and the erythrocytes 4,260,000; the hemoglobin was 74 per cent. The prostate was moderately hypertrophied; the urine contained a trace of albumin and leukocytes. The tonsils were small but contained cheesy plugs. The throat was moderately congested; there was moderate pyorrhea and retraction of the gums.

One rabbit was injected intracerebrally with a suspension from the tonsil, and one with a nasopharyngeal swabbing obtained November 17. Both developed attacks of spasms of the abdominal muscles and diaphragm. The spasms in both continued until death, and cultures from the brain yielded a pure growth of

the green-producing streptococcus. The plating of the nasopharyngeal swab showed countless numbers of colonies of green-producing streptococci. A single colony was inoculated into warmed glucose brain broth and rapidly transferred four times and then injected intracerebrally into two guinea-pigs. Both developed marked spasms of the diaphragm. The filtrate of nasopharyngeal washings, obtained November 17, was injected immediately intracerebrally into two rabbits, one receiving 1.5 cc. and the other 2 cc. Both developed clonic spasms of the

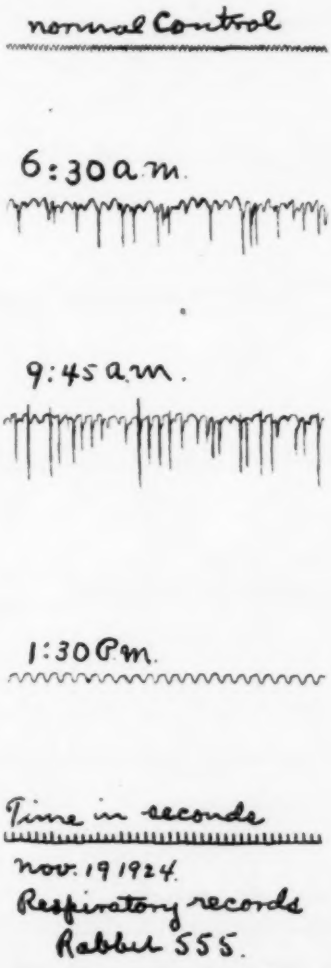

Fig. 4 (rabbit 555).—Intracerebral injection Nov. 17, 1924, with 0.2 cc. of the suspension of nasopharyngeal swabbings, case 2. The rhythmic spasms of the diaphragm at 6:30 and 9:45 a. m., and normal respiration at 1:30 p. m., following injection of encephalitis immune serum, may be noted.

muscles of the jaws, neck, shoulders, abdomen and diaphragm (fig. 5 *c*, *d* and *e*). Both recovered. A portion of this filtrate was put aside in the ice chest and injected, December 8, into one rabbit, producing marked spasms of the muscles, including spasms of the diaphragm. A second series of experiments was per-

formed December 8, three weeks after the hiccup disappeared. Two rabbits were again injected with the suspension of nasopharyngeal swabbings; neither developed muscular spasms. One remained free from symptoms the other showed weakness of the muscles of the neck and forelimbs, ataxia and peculiar movements of the head. It recovered from the weakness in the course of a week, but peculiar head movements simulating spasmodic torticollis persisted. The filtrate

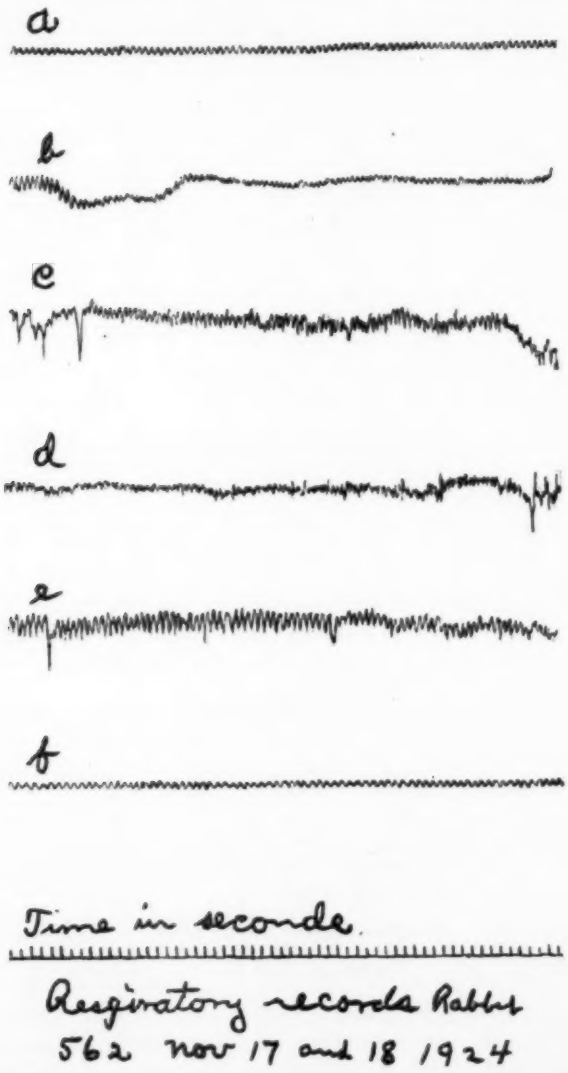

Fig. 5 (rabbit 562).—Intracerebral injection Nov. 17, 1924, at 5:30 p. m., with 1.5 cc. of filtrate of nasopharyngeal washings from case 3, at the time of the attack of hiccup; *a*, November 17, 7:30 p. m.; *b*, November 17, 7:45 p. m.; *c*, November 17, 8:30 p. m.; *d*, November 17, 9:30 p. m.; *e*, November 17, 10 p. m.; *f*, November 18, 9 a. m. The spasms of diaphragm and abdominal muscles in tracings *c*, *d* and *e* and normal respirations in *a*, *b*, and *f* may be noted.

from the nasopharyngeal washing, made exactly as during the patient's attack, the same solution of sodium chloride being used, was injected intracerebrally into three normal rabbits, and into two that had received the filtrate November 17 and had completely recovered. Four remained free from the tremor, twitchings and muscular spasms (fig. 6). One normal rabbit manifested slight tremor and twitchings of the masseters, lasting several hours. None had late symptoms.

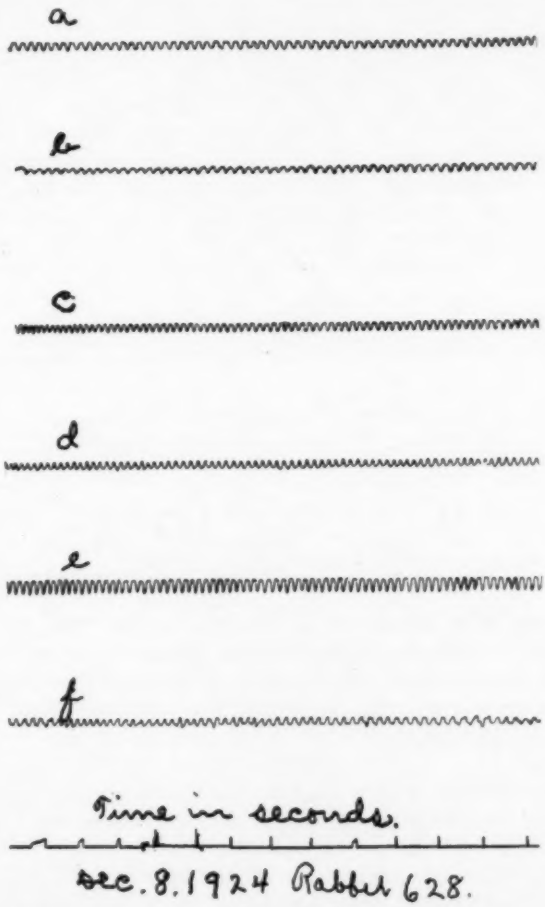

Fig. 6 (rabbit 628).—Injection Dec. 8, 1924, at 4:30 p. m., with 1.5 cc. of filtrate of nasopharyngeal washings, case 3, three weeks after recovery from hiccup; *a*, December 8, 7:30 p. m.; *b*, December 8, 7:45 p. m.; *c*, December 8, 8:30 p. m.; *d*, December 8, 9:30 p. m.; *e*, December 8, 10 p. m.; *f*, December 9, 9 a. m. The normal respiratory excursions without spasms throughout the experiment may be noted.

Comment.—The points of greatest interest in this case were the prompt disappearance of hiccup after nasopharyngeal washing; the late occurrence of lethargy; the production of spasms of the diaphragm and other muscles with the streptococcus in the nasopharyngeal and tonsillar

material, as well as after four rapidly made subcultures; the consistent occurrence of tremor and spasms of muscles, including the diaphragm, following injection of the filtrate of nasopharyngeal washings at the time of the attack, and the absence of these symptoms in identical experiments three weeks after the patient recovered.

CASE 4.—A man, aged 29, a patient of Dr. Neumann of Lewiston, Minn., felt badly on the morning of November 18. The following morning he was weak and shaky on getting up. Examination revealed slight fever, a slow pulse, marked tremor and ataxia, anxious facies and incoherent speech; in the afternoon and evening there were marked twitchings and spasms of the muscles. During the following night the patient vomited repeatedly, and was unconscious by 7 o'clock the next morning. At 11 oclock I found him in deep coma. He was very pale; the extremities were cold, the nails cyanotic; the eyes rolled back and the pupils were widely dilated but equal; the breathing was stertorous associated with breath holding and recurring vomiting attacks, and there was marked spasticity and rigidity of the arms and legs. The patient held his jaws rigid, making

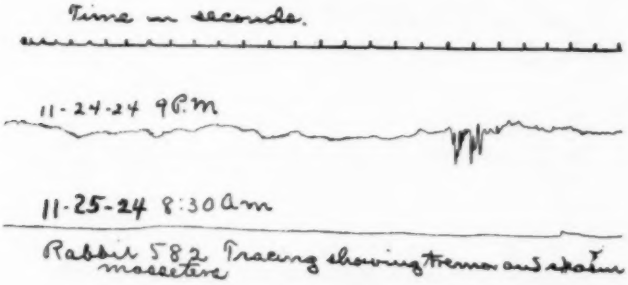

Fig. 7 (rabbit 582).—Intracerebral injection Nov. 24, 1924, 11:50 a. m., with 0.2 cc. of the glucose brain broth culture of the streptococcus after five subcultures and one animal passage, case 4. The fine continuous tremors and showers of spasms of masseters at 9 p. m. and their absence the following morning after administration of encephalitis immune serum may be noted.

inspection and swabbing of the throat impossible. He ground his teeth violently at intervals and had marked tremor and spasms of the masseters. The twitchings of the masseters, while almost continuous, varied greatly in intensity and occurred in showers similar to those that developed in rabbits injected with a culture from his nasopharynx (figs. 7 and 8).

The spinal fluid was under pressure; 40 cc. was removed. It was clear and contained 44 cells, mostly leukocytes. The pulse rate was 64 a minute; the temperature was 101 F.; the leukocytes numbered 13,000, and the urine was normal. The Wassermann reaction of the blood and spinal fluid was negative. Twenty cubic centimeters of my antipoliomyelitis serum was injected slowly, intravenously. No untoward symptoms followed, and one hour later undoubted improvement had occurred. The rigidity of the extremities and twitchings of the masseters was less marked, and the vomiting had disappeared. The serum treatment was repeated twice a day for three days. November 22, the patient had practically recovered. All the spasms had disappeared, likewise the rigidity of the extremities, the tremors and twitchings of the masseters; vomiting did not

recur; consciousness had returned and no paralysis of muscle groups could be elicited. Recovery was complete.

The patient's attack began as an epidemic of hiccup was passing through that region. On the day he became ill, a man living across the street developed hiccup from no apparent cause and it persisted for five days. Several nasopharyngeal swabs were made through the nostril of this patient. Suspension was made in the usual way, and two rabbits were injected intracerebrally. No symptoms developed. Only a few colonies of indifferent streptococci developed on blood-agar plates. One of the colonies was used to inoculate warmed glucose brain broth after the plates had been incubated for fifteen hours. The culture in the brain broth after five rapidly made subcultures, during forty-eight hours, was injected into the two rabbits that had remained well following inoculation of the swabbings. One was found dead the following morning. The other manifested marked rigidity of the muscles of the jaw and neck, violent grinding of the teeth, tremor and twitching of the masseters and clonic spasms of the muscles over the back and abdomen, lasting for two days, when 5 cc. of the serum used for the patient was given intravenously. Within an hour, tremor,

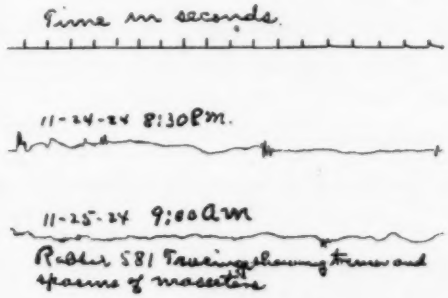

Fig. 8 (rabbit 581).—Intracerebral injection Nov. 24, 1924, 11:45 a. m., as in rabbit 582 (fig. 7). The extremely fine continuous tremor and showers of twitchings of masseters at 8:30 p. m. and 9 a. m. the following morning, not being relieved by administration of normal horse serum, may be noted.

spasm and rigidity had disappeared. A second injection of serum was given the next day, and the animal remained free from spasms but died two days later from paralysis. The culture in glucose brain broth of the strain isolated from the brain of this rabbit was injected into three rabbits. All showed similar symptoms consisting of irregular respiration, moderate hyperpnea, extreme rigidity of the jaws and tremor and twitchings of the masseters which occurred in paroxysms. (figs. 7 and 8). None had generalized myoclonic spasms or spasm of the diaphragm. Two were treated with the encephalitis serum, 5 cc. being given twice intravenously. Tremor and twitchings of the messeters disappeared promptly and permanently in both (fig. 7). One was treated in the same way with normal horse serum but without effect (fig. 8).

The washed and heat-killed (60 C., one hour) streptococcus, after five subcultures and one passage through an animal in physiologic sodium chloride suspension of the density of the glucose brain-broth cultures, was then mixed with equal parts of physiologic sodium chloride solution, encephalitis immune serum and normal horse serum, respectively, and incubated at 37 C. for three hours. Two rabbits were then injected with each of the three suspensions, each

receiving 1 cc. intracerebrally. Plate cultures of the suspensions, made at the time of injection, yielded approximately equal numbers of colonies in each. The two receiving the organisms treated with the immune encephalitis serum remained free from symptoms, while each of the four receiving the organisms treated with physiologic sodium chloride solution and normal horse serum developed tremors and spasms of the masseters, and muscles of the neck and shoulders. The strain isolated from positively affected animals was agglutinated specifically in high dilution by both the poliomyelitis and encephalitis-antistreptococcus serums. A positive precipitin reaction was obtained in these serums with the cleared nasopharyngeal swabbings, at the height of the attack. Three weeks later animal inoculations and precipitin reaction with nasopharyngeal swabbings proved negative.

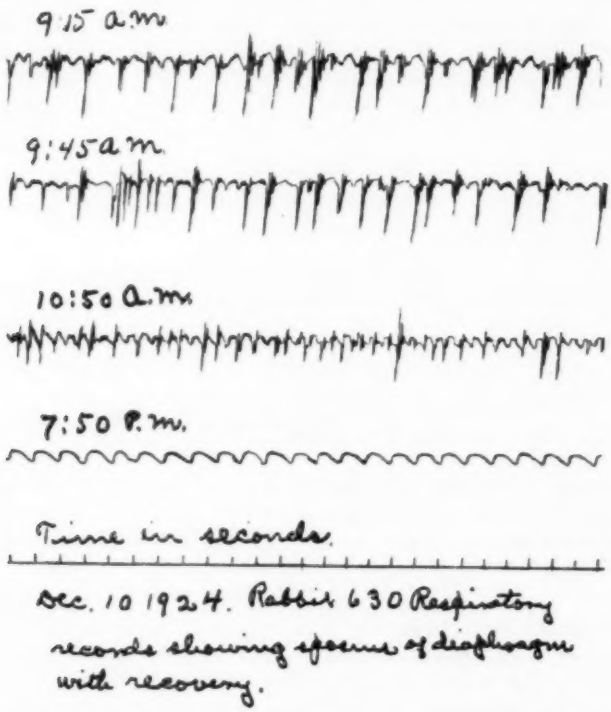

Fig. 9 (rabbit 630).—Intracerebral injection Dec. 10, 1924, with 0.1 cc. of the nasopharyngeal swabbing. The marked spasms of the diaphragm and abdominal muscles before treatment, and normal respiration after treatment with the encephalitis serum, may be noted.

Comment.—The points of particular interest in this case of myoclonic encephalitis are the clinical history suggesting its relationship to epidemic hiccup; the results of experiments on animals in which the condition in the patient was closely simulated; the positive precipitin reaction with nasopharyngeal swabbings at the height of the attack; the marked agglutination of the strain isolated from animals that developed encephalitis with the poliomyelitis and encephalitis hyperimmune horse serums;

the prompt relief from symptoms in the patient and in the rabbits following treatment with both the poliomyelitis and the encephalitis immune serums, and no effect in animals treated with normal horse serum; the absence of symptoms in the animals injected with the heat-killed organisms after treatment with the encephalitis immune serum, and the muscular tremors and spasms that developed on the injection of the dead organisms after treatment with physiologic sodium chloride solution and normal horse serum.

CASE 5.—A man, aged 54, came to the clinic Nov. 4, 1924, on account of weakness in the legs, especially the right, and pain in the arms and across the shoulders, which had persisted for three months, and on account of symptoms of spondylitis of longer standing. There was no rectal disturbance but urination had become slow. General examination showed that the patient was well developed and well nourished. His spine was rigid from chronic spondylitis. There was tenderness over the chest and shoulders. The right pupil was larger than the left. The teeth were septic and the tonsils small but infected. The liver was enlarged two fingers below the costal arch, smooth, not tender. There was paralysis of the right leg of the flaccid type, and weakness in the left leg, with exaggerated reflexes. There were no Babinski signs, and no edema. Roentgenologic examination of the chest and spine showed hypertrophic arthritis in the cervical and dorsal regions, with no evidence of malignancy.

While the patient was under observation in the hospital a gradually increasing and painless jaundice, enlargement of the liver and a palpable mass in the region of the gallbladder appeared. The leukocytes numbered 8,500, and the erythrocytes 4,400,000; the hemoglobin was 75 per cent. The Wassermann reaction of the spinal fluid and of the blood was negative. The spinal fluid showed 4 lymphocytes for each cubic centimeter. Urinalysis revealed negative findings; the temperature was normal. Incessant vomiting began the morning of December 4, and continued for two days. The blood chlorides, blood urea and carbon dioxide combining power of the blood were normal. From December 6 to 8, after the vomiting had ceased, the patient felt better and took a moderate amount of nourishment. Hiccup, which had been slight for two days, became persistent. Hypodermics of morphine and other sedatives gave no relief. December 9, at 10 p. m., 20 cc. of anti-encephalitic serum was given intramuscularly. The hiccup disappeared three hours later, and the patient slept the rest of the night. December 10, at 9:30 a. m., 20 cc. of the serum was injected intramuscularly, and at 7:30 p. m., 25 cc. The hiccup did not return. The patient went home December 11, and word was received that he died December 25.

In order to determine, if possible, the cause of the hiccup, and possibly other symptoms of central origin, the suspension of the nasopharyngeal swab obtained December 9 was injected intracerebrally into two rabbits in the usual manner. The rabbit receiving 0.2 cc. showed tremor of the masseters, clonic spasms of the muscles of the neck and shoulders and marked weakness of the forelimbs within ten hours, and was found dead the following morning. Cultures from the brain yielded large numbers of green colonies of streptococci. The one receiving 0.2 cc. had developed marked spasms of the diaphragm and abdominal muscles in twenty hours (fig. 9, 9:15 a. m.), associated with hiccup during the more severe spasms. It was then given 5 cc. of normal horse serum intravenously. The spasms continued undiminished for thirty minutes (fig. 9, 9:45 a. m.). At 10:15 a. m. they had not abated, and the rabbit was given 5 cc. of the encephalitis

serum. Within thirty-five minutes the spasms had become much less severe (fig. 9, 10:50 a. m.), and hiccup had disappeared. The injection was repeated. The spasms grew gradually less severe and occurred less often, and by 7:50 p. m., had disappeared entirely (fig. 9). They remained absent, and the animal was completely relaxed during three additional hours of observation, but was found dead the following morning. Necropsy revealed small hemorrhages in the medulla and moderately turbid spinal fluid and several hemorrhages in the nerve trunks of the brachial plexus. Cultures from the brain and cord showed that the streptococcus had disappeared and that accidental invasion with the *Bacillus bronchisepticus* had occurred.

Comment.—Carcinoma of the biliary tract and liver was believed to be the cause of the jaundice, and chronic infective arthritis the cause of the changes in the spine. The pain and tenderness in the arms and shoulders, the paralysis of the right leg, the numbness and weakness of the left leg, the disturbance of the bladder and the attack of nausea and vomiting and hiccup were considered manifestations of infective neuritis and myelitis. The animal experiments and the fact that an epidemic of hiccup and other cases presenting similar symptoms occurred at the time suggest that the infective agent was the streptococcus isolated at the time of the attack of hiccup. The close relation of this streptococcus to the streptococcus of encephalitis is indicated by the fact that spasms of the diaphragm and hiccup of the patient and animals disappeared promptly following administration of the encephalitis immune serum.

CASE 6.—A man, aged 43, had intermittent hiccup during the night of Dec. 30, 1924. The following day he vomited several times, and had a feeling of distress in the stomach. The attacks of hiccup recurred frequently, lasting from twenty minutes to one hour. The spasms became violent causing pain and exhaustion. The patient had had double vision for one day. The leukocytes numbered 11,000. The temperature and pulse were normal. On the evening of December 31, he was given 10 cc. of the concentrated encephalitis immune serum. He slept most of the night. The nausea, distress in the stomach and double vision did not return the following morning, but he continued to have short intervals of slight hiccup. He was then given two injections of 20 cc. each of the concentrated serum; coincidentally the hiccup disappeared permanently, and he felt well.

SUMMARY AND CONCLUSIONS

The results of my previous studies have been verified in detail in two additional series of cases. A streptococcus, alike in morphology and with similar cultural characters and having similar immunologic reactions, was isolated from the infection atrium in twenty additional cases of epidemic hiccup, and with each strain, spasms of the diaphragm or other muscles were produced in animals. The organism was isolated from these animals and characteristic symptoms again induced on inoculation. It was demonstrated in the lesions, and proved absent elsewhere, by microscopic examination of sections. Similar experiments, made with streptococci from cases of poliomyelitis and other diseases of the

nervous system, from poliomyelitis contacts, from normal controls and from patients that had recovered from hiccup, gave strikingly different results. The possibility of an accompanying filterable virus (in the usual meaning of that term) being the cause of the spasms was excluded by the successful reproduction of characteristic symptoms with some of the strains after many rapidly made subcultures, with the dead streptococci, and with filtrates of active cultures, the symptoms in the case of filtrates beginning in from one to three hours after injection.

Positive results were obtained by methods in which the conditions in patients were closely simulated, as well as by intracerebral inoculation of cultures, in some instances in more than one species of animal. Packing of the nose with gauze soaked in cultures sufficed to provoke spasms of the diaphragm and other muscles. Of the common laboratory animals, rabbits were found most susceptible, but similar results were sometimes obtained in guinea-pigs and monkeys (*Macacus rhesus*). The streptococcus produces in the throat of the patient, as in cultures, a filterable substance which has the power of inciting spasms of the diaphragm and other muscles. The type of disease and the lesions induced were in many respects similar to those noted in the spontaneous disease. The spasms of the diaphragm have been seen through an incision in the abdominal wall made under local anesthesia, and by means of the fluoroscope. They were usually severe, and continued for hours and sometimes days. In the animals, as in man, synchronous spasms of the abdominal muscles frequently occurred, as suggested by Dr. Hugh Patrick. During the severe spasms audible hiccup was frequently noted in rabbits and monkeys. Cadham has verified my previous results and has produced myoclonic spasms of the diaphragm with five of sixteen strains of the streptococcus isolated from patients having epidemic hiccup, in Winnipeg. The conclusion that epidemic hiccup is due to a streptococcus (*Streptococcus singultis*) having peculiar neurotropic properties seems warranted.

The close relationship believed to exist between epidemic hiccup and epidemic encephalitis, and indicated by epidemiologic findings, receives much support in these experiments. The symptoms and lesions in the animals that succumbed were similar to those in fatal cases of hiccup reported in the literature. In some instances, especially after one or more passages through animals, and after many subcultures, the streptococcus from cases of hiccup no longer produced spasms of the diaphragm but instead lethargic or other forms of encephalitis (table 1). Spasmodic torticollis, which developed as a late manifestation, was as common in the hiccup series as in the encephalitis experiments. The strains from the two diseases, culturally indistinguishable, are cross agglutinated and the cleared nasopharyngeal extracts in a sodium chloride solution cross precipitated by the respective antistreptococcus serums; and the encepha-

litis hyperimmune horse serum had marked curative effects in animals having spasms of the diaphragm following injection of the streptococcus from cases of hiccup. The results from serum and vaccine treatment of cases, while striking, are far too few to be conclusive. The facts, however, that the serum had a marked curative effect on animals under controlled conditions, that normal horse serum had no effect and that active immunization afforded protection for rabbits injected with the hiccup streptococcus, afford a rational basis for the attempts at passive and active immunization.

A CASE OF HYDROPHOBIA WITH NEGRI BODIES IN THE BRAIN

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Hydrophobia is such an uncommon disease that very few papers have appeared in recent years on the clinical aspect of this disease or on the pathologic findings in the human brain. Most of the work on the subject has been done on animals. The view is now generally held that the presence of Negri bodies in the brain of an animal is pathognomonic of rabies. They have rarely been found, however, at least as far as the literature on the subject is concerned, in the human brain. It is still uncertain whether the bodies described by Negri in 1903 are the true etiologic agents in the production of the disease. Their reported cultivation by Noguchi in 1913 has not been confirmed, so far as I can learn, by other workers, nor has Noguchi continued his experimental studies on these interesting bodies.

Although the following case came to my attention only a few days before the death of the patient, through the cooperation of various physicians and the patient's family a fairly complete history of the important events in the illness are here recorded with the main features found at necropsy.

REPORT OF CASE

Mr. G., a shoe worker, aged 42, was first seen in the late afternoon of Sept. 14, 1923, in periodic, severe attacks of coughing and delirium. His present illness, so far as acute symptoms were concerned, dated from three days previously, when he came home from work tired and exhausted with a slight headache and stiffness of the right side of his neck and arm. He complained of pain in the same region. During the next twenty-four hours he was repeatedly nauseated, he vomited and his temperature rose to 100 F. His symptoms were consistent with a mild attack of influenza. On the next day, September 12, his temperature was normal, but he complained of a sore throat and difficulty in swallowing, a symptom which persisted until his death. His right arm felt numb. The gastric symptoms ceased. September 13, he left home against advice and visited a throat specialist who suggested to him the diagnosis of hydrophobia because the throat symptoms were more pronounced when he attempted to drink water. When the patient returned home he showed marked anxiety and said that he was sure he had hydrophobia. Attempts at persuasion by his family and physicians did not shake him from this belief. That evening he was able to drink hot milk, but cold water caused him to choke and increased his anxiety. In the opinion of two physicians who saw him that night, his symptoms were hysterical, partly induced by the suggestion offered by the diagnosis of hydrophobia.

On the afternoon of September 14, when I first saw the patient, he was greatly agitated, walking about the room calling out, "I can't swallow" and

"Can't you do something for me?" These periods of excitement were followed by a moment of rest, when he sat on the side of the bed, holding his head in his hands. Suddenly, throwing himself on the bed, he would roll about clutching at his throat and making hoarse, croaking noises, suggestive of an animal-like growl. The attack, lasting perhaps a minute, was followed by an exhausted period, the whole cycle taking about five minutes. Between attacks he seemed to realize his condition fully, and told me that he could feel the attacks coming on and that they were made distinctly worse by the sight of a glass of water or the sound of running water. When I asked him more definitely about the cough, he became angry and accused me of bringing tobacco smoke into the room to annoy him and make his spasms worse. He smelled smoke on my clothes although I had not been smoking for some hours. He also said that he could see it in the room. Practically no physical examination of the patient could be made. An attempt to look at his eyes threw him into spasm. The deep reflexes of the legs were equal and active and there was no clonus or Babinski sign.

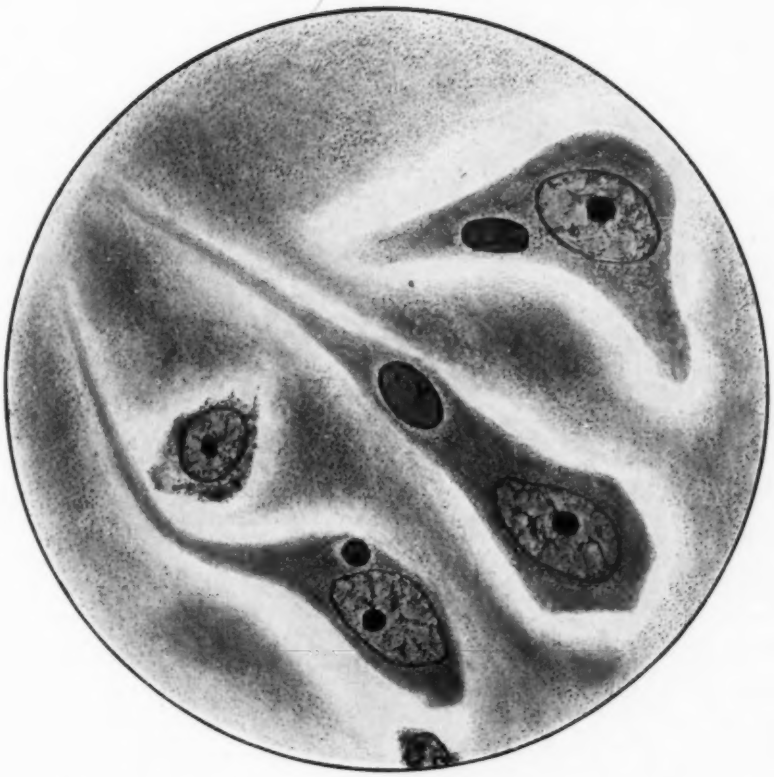
The past history was of great importance in making the diagnosis. Jan. 29, 1923, the patient was bitten on his right thumb by a pet dog, the injury causing severe bleeding. The dog had been ill for about one week, showing signs of bad temper and a tendency to snap at objects and persons. The dog ate poorly, had difficulty in drinking water and frothed at the mouth two or three days before he died. He died at home the day after he bit the patient. A veterinarian saw the animal on January 28, but took no action. No examination of the brain was made after death.

The wound on the patient's thumb healed slowly, but treatment by a physician was not considered necessary. The patient complained of marked sensitiveness of the wound for some months after the injury. During the summer the patient's wife noticed signs of increasing nervousness in her husband, which she attributed to financial difficulties and lack of steady employment. By August, the patient had noticed his increasing susceptibility to sudden noises or flashes of light. The passing of a train on an adjacent railroad track so annoyed him that he figured out the exact time his commuter's train would pass other trains on the road, so that he could "brace himself" when the noise occurred. He would cross over to the other side of the train, at times, to avoid the jar. A glaring light was an annoyance to him. His sense of smell also became over-sensitive. He was easily startled.

He was sent to the Boston Psychopathic Hospital immediately after he was seen. I am indebted to that hospital for a continuation of this report.

He entered the hospital after riding twenty miles by automobile. His temperature was 106 F. Swallowing was impossible except for small amounts of warm liquid, because of almost continuous spasm of the muscles of deglutition. He became violent, talking incessantly about his work and complained about his employer; then he would switch to an outburst against his wife, who was in the room, accusing her of being unfaithful and even attempting to attack her, so that it was necessary for her to leave the room. During his delirium he was keenly alive to what was going on about him. Five minutes before death he stiffened out in a tonic spasm, his head in moderate opisthotonos, his breathing quick and shallow. The contraction and locking of his laryngeal muscles could be seen. He died in this spasm without relaxation.

Necropsy by the medical examiner gave practically negative results except for the findings in the brain. The mucous membranes of the throat, esophagus and stomach showed evidence of capillary hemorrhage. Negri bodies were



Cells from the hippocampus stained with eosin and methylene-blue showing the Negri bodies within the ganglion cells. The variety of size and shape of the bodies and their large size in relation to the cells may be noted.

easily demonstrated from direct smears of the hippocampus as well as from section as shown in the figure. The brain showed no change on gross examination.[1]

COMMENT

The case conforms clinically to the usual description of hydrophobia except for the long duration of the incubation period and the insidious onset of the symptoms. The ease with which Negri bodies were demonstrated in the brain may also be considered unique. The period of incubation is extremely variable, averaging from six weeks to two months. It is rarely prolonged to three months. In this case death occurred more than seven months after inoculation. Premonitory symptoms, however, began about five months after the patient was bitten.

The symptoms began insidiously, with increasing degrees of hyperesthesia. The patient was irritable, sleepless, depressed and over-anxious for nearly two months before death. So common, however, are these symptoms in other diseases that the true diagnosis was overlooked. Pain in the wound might have suggested hydrophobia, as it is usually the earliest and is also the most common symptom. Only at the approach of the stage of excitement, four days before death, was the correct diagnosis made, mainly on a basis of the reflex spasm of the throat. Death occurred in the stage of excitement, there being no paralytic stage.

Negri bodies have been found in the brains of 98 per cent of rabid animals and have not been demonstrated in other diseases. Their demonstration in the brain of an animal is now considered sufficient proof of rabies.[2] They were first described by Negri who was working in Golgi's laboratory in Pavia.[3] Few descriptions are found in the literature of the bodies in the human brain. Those figured here conform to the bodies originally described.

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1. I am indebted to Dr. R. F. Rauscher for part of the clinical notes and to Dr. W. J. Brickley for the pathologic specimens.

2. Mohler, J. R.: Rabies or Hydrophobia, Farmers Bull. 449, U. S. Dept. Agric.

3. Negri, Adelchi: Ztschr. f. Hyg. u. Infectionskrankh. **43**:507, 1903.

SIGNIFICANT CHEMICAL CHANGES IN THE SPINAL FLUID IN MENINGITIS

WITH SPECIAL REFERENCE TO LACTIC ACID CONTENT *

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In 1917, Tashiro and Levinson [1] reported observations on the differential precipitation of the proteins of the spinal fluid by alkaloidal and metallic precipitants in tuberculous and epidemic meningitis, and miscellaneous pathologic conditions. The convenient method of differential diagnosis between tuberculous and epidemic meningitis proposed by these authors is briefly described as follows: Three small, narrow-bored test tubes are prepared, and in them separately are placed 1 cc. of 3 per cent sulphosalicylic acid, 1 cc. of 1 per cent mercuric chloride and 1 cc. of 0.5 per cent phenolphthalein rendered slightly pink by the addition of dilute sodium hydroxide. To each tube is added 1 cc. of the spinal fluid; the contents of the tube are thoroughly mixed, and the tubes stoppered with cotton and allowed to stand for twenty-four hours. Specimens of spinal fluid from normal persons give a faint turbidity with sulphosalicylic acid and no change with the mercuric chloride, the pink of the phenolphthalein becomes more pronounced on standing. The increasing pink of the phenolphthalein indicates a decreasing acidity, due to the escape of carbon dioxide. All meningitic fluids show a turbidity with the alkaloidal precipitant as soon as the spinal fluid is added to the reagent, but a differentiation between tuberculous and epidemic meningitis is made by observing the ratio between the alkaloidal and metallic sediments after the precipitated fluids have been standing for twenty-four hours. In tuberculous meningitis the sediment of the mercuric chloride precipitation is usually twice the height of the sulphosalicylic acid precipitation. In epidemic meningitis, on the other hand, the mercuric chloride precipitation is slight and the sulphosalicylic acid precipitation is marked, the ratio being 1:2 or 1:3.

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* Read in part before the American Neurological Association, Washington, D. C., May 4, 1925.

1. Tashiro, S., and Levinson, A.: J. Infect. Dis. **21**:571 (Dec.) 1917.

MENINGITIS AND ENCEPHALITIS

Since the appearance of this publication, 250 specimens of spinal fluid have been studied by us. Of this number twenty-four were from cases of tuberculous meningitis, and thirty-one from cases of meningococcus meningitis. In all of these instances the diagnosis was based on the demonstration of the bacteria in the spinal fluid. The remainder represented fluids from miscellaneous cases such as meningitis due to other bacteria, encephalitis, cerebrospinal syphilis and meningismus. The results are summarized by the data on representative cases in tables 1

TABLE 1.—*Protein Precipitation of Spinal Fluid*

Case	Age Yr.	Age Mo.	Sulphosalicylic Acid, Mm. of Precipitate	Mercuric Chloride, Mm. of Precipitate	Phenolphthalein	Sugar, per Cent	Carbon Dioxide Combining Power, per Cent by Volume	Remarks
F. A.	..	7	Turbid	4	Colorless	0	44.7	Tuberculous meningitis
W. P.	5	9	Turbid	4	Colorless	0	43	Tuberculous meningitis
J. F.	1	1	4	6	Pink	0.041	44	Tuberculous meningitis
D. L.	6	..	2	4	Colorless	0	57	Tuberculous meningitis
D. R.	2	10	4	1	Colorless	0.041	33	Meningococcus meningitis
E. R.	8	..	3	5	Colorless	0	28	Meningococcus meningitis after serum
B. A.	1	11	4	Turbid	Pink	0.045	52	Meningococcus meningitis
			5	Turbid	Pink	0.059	48	
			3	5	Pink	0.084	52	After serum

TABLE 2.—*Protein Precipitation of Spinal Fluid*

Case	Age, Years	Sulphosalicylic Acid, Mm. of Precipitate	Mercuric Chloride, Mm. of Precipitate	Phenolphthalein	Sugar, per Cent	Carbon Dioxide Combining Power, per Cent by Volume	Remarks
K. F.	1½	4	5	Pink	0.090	36	Encephalitis; dead
L. F.	44	1	2	Pink	0.088	..	Encephalitis; improved
G. H.	36	0	Turbid	Pink	0.083	48	Encephalitis
T. L.	20	3	6	Pink	0.076	54	Encephalitis
A. B.	8	4	1	Colorless	0	30	Streptococcus hemolyticus meningitis; died
J. L.	14	12	27	Colorless	0	35	Staphylococcus and pneumococcus meningitis
M. F.	1½	7	11	Pink	0.093	42	Brain abscess; no bacteria
W. L.	3	15	16	Colorless	0	43	Streptococcus meningitis; died

and 2. In general it may be said that our findings for tuberculous and meningococcus meningitis agree with those reported by Tashiro and Levinson. Subjects E. R. and B. A. of table 1 illustrate a point stressed by these authors. The administration of serum intraspinally in meningococcus meningitis disturbs the ratio of the precipitates by the two precipitants so that the readings are practically reversed. Case E. R., gave 5 mm. of precipitate with mercuric chloride and 3 mm. with sulphosalicylic acid after serum was introduced intraspinally, although meningococci had been found in the fluid. Case B. A. before the introduction of the serum showed 4 mm. of precipitate with sulphosalicylic acid,

and the following day 5 mm.; but the mercuric chloride produced only a turbidity in the fluid. However, after the serum therapy, the ratio was changed to 3: 5.

The cases of encephalitis (table 2) show ratios for the precipitates with the two reagents similar to those observed in tuberculous meningitis. However, in encephalitis the figures for the spinal fluid sugar are higher than those of tuberculous fluids. In the case of streptococcus hemolyticus meningitis (case A. B. of table 2) the precipitation of the protein corresponds to quantities and ratios of epidemic meningitis, but the following three cases more closely resemble tuberculous meningitis in the ratios of precipitates. However, in these latter three fluids the quantities of protein precipitated far exceed those found in tuberculous meningitic fluids. In the three purulent meningitic fluids (A. B., J. L. and W. L., table 2), the pink of the phenolphthalein was dispelled, and no reaction for sugar was obtained. However, subject M. F. presented an abnormally high figure for sugar, and a normal reaction with phenolphthalein.

Levinson [2] attributed this observed difference of the response of the proteins to the precipitants to a variation in the reaction of the spinal fluid. He noted that the hydrogen ion concentration of the spinal fluid increased on standing exposed to air, but if preserved tightly stoppered it did not change. Fluids from cases of tuberculous meningitis were similar to normal fluids in this respect, but the increase in alkalinity was more rapid on standing, as a result of a greater amount of carbon dioxide liberated. Cases of epidemic meningitis show a lowering of the hydrogen ion concentration corresponding to the severity of the disease, and it may further decrease on standing. In these latter cases the increase of the hydrions was attributed to a production of lactic acid. In the cases reported in the tables, the pink of the phenolphthalein tube was dispelled by the tuberculous fluid, but in many instances the color returned and grew more intense after standing for about five hours at room temperature. The observations concerning the color of this tube have been made at the end of the five hour period. It will be observed, however, that of the three cases reported in the table two remained colorless. In these two instances no sugar reaction was obtained in the fluids. Of the other cases of meningitis reported, similar findings are noted: where the sugar of the spinal fluid has been decreased to a negative reaction there appears with this rough qualitative test an increase in acidity. Case D. R. of table 1 appears as an exception. The sugar concentration of the fluid here was 41 mg. per hundred cubic centimeters but the phenolphthalein showed an alkaline reaction. There appears to be no demonstrable relation between the carbon

2. Levinson, A.: J. Infect. Dis. **21**:556 (Dec.) 1917.

dioxide combining power of the spinal fluid and its reaction with phenolphthalein.

Since Levinson has attributed the evidently fixed decrease in alkalinity of the spinal fluid in meningococcus meningitis to a production of lactic acid and the temporary decrease in tuberculous meningitis to carbon dioxide, a study has been made of the lactic acid and sugar concentration of the spinal fluid in the meningitides. For the determination of lactic acid Clausen's method [3] has been employed, utilizing the permanganate method of oxidation. Nishimura [4] has emphasized some of the possible sources of error in the use of this method, and the steps outlined by him have been followed. The Folin-Wu [5] method was used for sugar determinations. The spinal fluids were obtained by lumbar puncture after at least a fifteen hour fast and analyzed immediately.

Specimens of spinal fluid were obtained from four apparently normal persons at rest and during the fasting state (table 3). These fluids

TABLE 3.—*Sugar and Lactic Acid of Normal Spinal Fluids*

Subject	Sugar, Mg. per 100 Cc.	Lactic Acid, Mg. per 100 Cc.	Leukocytes, per C.mm.
J. B.	65	8.1	4
T. P.	70	9.4	10
N. P.	54	7.2	7
E. N.	75	6.3	5

gave no pathologic findings with the usual chemical tests. The sugar ranged from 54 to 75 mg. per hundred cubic centimeters and the lactic acid from 6.3 to 9.4 mg. per hundred cubic centimeters.

SUGAR AND LACTIC ACID CONTENT

There appears in the literature a diversity of opiniqns concerning the sugar concentration of normal spinal fluid. Critical examination shows that much of these data is not for the spinal fluids of normal persons but for miscellaneous pathologic conditions presenting no meningeal symptoms. Coope [6] reports 64, 69 and 83 mg. of glucose per hundred cubic centimeters of spinal fluid in three normal cases. The sugar content of the spinal fluids of normal children was reported by Schloss and Schroeder [7] from 50 to 139 mg. per hundred cubic centimeters. In ten

3. Clausen, S. W.: J. Biol. Chem. **52**:263 (May) 1922.

4. Nishimura, K.: Proc. Soc. Exper. Biol. & Med. **22**:322, 1925.

5. Folin, O., and Wu, H.: J. Biol Chem. **41**:367 (March) 1920.

6. Coope, R.: Quart. J. Med. **15**:1 (Oct.) 1921.

7. Schloss, O. M., and Schroeder, L. C.: Cerebrospinal Fluid, Am. J. Dis. Child. **11**:1 (Jan.) 1916.

normal children Leopold and Bernhard [8] obtained an average of 70 mg. Wilcox and Lyttle [9] state that the available data warrant the statement that normally the sugar content of the spinal fluid is about one half that of the blood and that its range of variation corresponds to that of the blood. Goodwin and Shelley [10] have shown that the daily variation of sugar of the spinal fluid for any person after a night's fast may be from 4 to 15 mg. per hundred cubic centimeters. These authors state that there is no level within reasonable limits which might be considered normal for different persons, but that there is a definite relationship between the sugar content of the cerebrospinal fluid and that of the blood. Expressed as a percentage relationship of the sugar content of the cerebrospinal fluid to the sugar content of the blood, this ratio lies between 45 and 65 per cent. In six normal cases Thalheimer and Updegraff [11] report spinal fluid sugars from 53 to 74 mg. (from 40 to 48 per cent of the blood sugar). Myers and Fine [12] have compared the sugar concentration of the spinal fluid with that of the blood in fifteen cases representing various degrees of severity of nephritis. These authors found that the sugar of the spinal fluid amounted to about 60 per cent of the quantity present in the blood.

In table 4 are recorded the data on the lactic acid and sugar of the spinal fluid of twenty-four cases representing miscellaneous pathologic conditions, including meningismus. It is seen that, although there is considerable variation in the figures for the sugar, none is below the level considered normal. On the other hand, a number of fluids show unusually high figures for sugar. Case S. C. has a spinal fluid sugar of 104 mg. which was coincident with a hyperglycemia associated with streptococcus hemolyticus bacteremia. The hyperglycemia and the increased sugar of the spinal fluid may be due to the blood stream infection, since Hirsch [13] has shown that the injection of pathogenic bacteria into animals provokes hyperglycemia. Subject J. B. shows an unusually high spinal fluid sugar of 94 mg. The diagnosis established at necropsy was malignant teratoma of the testis with metastasis to the brain. A high spinal fluid sugar in cases of brain tumor has been reported by Thalheimer and Updegraff, and by Wilcox and Lyttle. However, the other two cases of brain tumor have spinal fluid sugars well within

8. Leopold, J. S., and Bernhard, A.: Chemistry of Spinal Fluid, Am. J. Dis. Child. **13**:34 (Jan.) 1917.

9. Wilcox, H. B., and Lyttle, J. D.: Arch. Pediat. **40**:215 (April) 1923.

10. Goodwin, G. M., and Shelley, H. J.: Sugar Content of Cerebrospinal Fluid and Its Relation to Blood Sugar, Arch. Int. Med. **35**:242 (Feb.) 1925.

11. Thalheimer, W., and Updegraff, H.: Sugar Content of Blood and Spinal Fluid in Encephalitis, Arch. Neurol. & Psychiat. **8**:15 (July) 1922.

12. Myers, V. C., and Fine, M. S.: J. Biol. Chem. **37**:239 (Feb.) 1914.

13. Hirsch, E. F.: J. Infect. Dis. **29**:40 (July) 1921.

normal limits. In these cases discussed, the lactic acid varied from 7.7 to 16.8 mg. per hundred cubic centimeters, but the majority of the figures were below 12 mg.

Six cases of encephalitis have been studied. The sugar content of these fluids varied from 46 to 72 mg. per hundred cubic centimeters. None showed the unusually high spinal fluid sugars reported in the literature by some authors for encephalitis. However, Cooper's careful review of the literature and his own observations show that a high spinal fluid sugar is by no means a constant finding in encephalitis. The lowest figure obtained for the lactic acid was 13.1 mg. and the highest 26.1. In the case J. S. (table 4), the lactic acid dropped within four days

TABLE 4.—*Sugar and Lactic Acid of Spinal Fluids of Miscellaneous Pathologic Conditions*

Patient	Age Yr.	Age Mo.	Sugar	Lactic Acid	Diagnosis
A. J.	14	..	79	16.8	Congenital cataract
C. Q.	49	..	66	13.9	Chronic cholecystitis
E. F.	42	..	69	11.3	Neuritis
W. J.	34	..	71	8.6	Cholecystitis
A. M.	3	5	55	11.3	Otitis media
S. C.	2	..	104	15.8	Peritonitis; streptococcus hemolyticus
J. R.	60	..	77	12.6	Arteriosclerosis; hemiplegia
R. T.	34	..	82	10.4	Anterior poliomyelitis (chronic)
F. G.	2	6	64	9.9	Brain tumor
B. R.	8	..	69	8.6	Brain tumor
J. B.	26	..	94	11.8	Brain tumor
E. G.	39	..	78	11.3	Epilepsy
M. A.	20	..	55	11.3	Epilepsy
W. H.	27	..	103	22.3	Chronic nephritis; after convulsions
S. S.	12	..	113	22.9	Chronic nephritis; after convulsions (alkalosis)
R. M.	3	..	72	7.7	Polioencephalitis
M. S.	7	..	66	13.1	Encephalitis
T. G.	12	.	48	17.1	Encephalitis
P. E.	14	..	69	13.0	Encephalitis
J. S.	26	..	46	26.1	Epidemic encephalitis
			72	18.0	Four days later
L. M.	9	12	68	23.2	Epidemic encephalitis
			61	17.5	Twenty-nine days later
S. H.	3	..	99	10.4	Meningismus with bronchopneumonia
K. L.	2	1	75	14.8	Meningismus with bronchopneumonia
I. F.	1	9	78	14.8	Meningismus with bronchopneumonia

from 26.1 to 18.0, but the sugar rose from 46 to 72 mg. In the following case the decrease in the lactic acid from 23.2 to 17.5 mg. was accompanied by a fall in the sugar from 68 to 61 mg. within a period of twenty-nine days.

In the four cases of epilepsy observed (cases E. G. and M. A., table 4, and B. A. and R. N., table 7) the sugar and lactic acid of the spinal fluid were found unchanged from the normal during the interval periods. In two instances (cases B. A. and R. N., table 7) spinal fluid was again obtained twenty minutes after the cessation of the convulsions, and those specimens withdrawn following the convulsions show an increase in both the sugar and the lactic acid. The lactic acid rise amounted to more than 100 per cent of the initial figure, but the increase in sugar was much less, from 67 to 88 mg. in one case and from 60 to

67 mg. in the other. The lactic acid increase in the spinal fluid, however, was out of proportion to the increase in the blood not only in the cases of epilepsy noted here but also constantly in others which we have examined. The significance of this cannot be hinted at now. Studies are being made of the hydrogen ion concentration, lactic acid and sugar content, and carbon dioxide combining power in both blood and spinal fluid in cases of epilepsy before and after convulsions. This work will be reported later.

This observed increase in lactic acid after the convulsions of nephritis and epilepsy is not confined to the spinal fluid. A comparison of the changes in sugar and lactic acid of the blood with those of the spinal fluid in these two conditions (cases A. W., B. A. and R. N., table 7) demonstrates that similar increases are observed in the blood. The

TABLE 5.—*Sugar and Lactic Acid of Spinal Fluids in Meningitis*

Patient	Age Yr.	Age Mo.	Sugar	Lactic Acid	Diagnosis
L. M.	6	..	0	54.3	Meningococcus meningitis; no treatment
H. D.	..	2	31	24.8	Meningococcus meningitis; no treatment
L. D.	..	..	10	24.8	Meningococcus meningitis; no treatment
F. M.	..	2	10	22.8	Meningococcus meningitis; no treatment
B. A.	..	10	84	22.5	Meningococcus meningitis; serum treatment for 22 days; died 9 days later
Y. B.	1	1	17	32.8	Influenzal meningitis; died
R. K.	..	..	23	31.0	Pneumococcus meningitis
E. Z.	6	..	0	23.4	Pneumococcus meningitis
A. M.	2	..	0	27.9	Streptococcus hemolyticus meningitis
G. C.	7	..	25	22.7	Tuberculous meningitis
A. O.	2	3	29	44.5	Tuberculous meningitis; pulmonary tuberculosis
S. H.	1	4	30	25.2	Tuberculous meningitis
G. McK.	..	..	25	24.1	Tuberculous meningitis
L. S.	..	..	25	25.6	Tuberculous meningitis
A. H.	..	..	10	33.7	Tuberculous meningitis; active pulmonary tuberculosis
J. A.	24	..	16	22.0	Tuberculous meningitis and miliary tuberculosis
C. S.	1	8	73	16.6	Tuberculous meningitis
			50	11.2	Twelve days later
M. G.	..	..	25	22.0	Tuberculous meningitis
M. D.	..	..	75	25.6	Tuberculous meningitis

increased production of lactic acid during nephritis and epileptic convulsions is in keeping with observations made by others after vigorous muscular contractions. Zweifel [14] isolated sarcolactic acid in considerable quantities from the maternal venous blood and the blood of the cord after eclamptic convulsions. Liljestrand and Wilson [15] prepared sarcolactic acid from the urine of normal persons following strenuous muscular exercise over a short period of time.

Three cases of meningismus associated with bronchopneumonia are reported. No significant variations were noted either in the sugar or in the lactic acid of the spinal fluid.

Observations made on the sugar and lactic acid of the spinal fluid in meningitis are reported in table 5. In the first four cases of meningo-

14. Zweifel, P.: München. med. Wchnschr. **53**:297, 1906.

15. Liljestrand, S. H., and Wilson, D. W.: J. Biol. Chem. **65**:773 (Oct.) 1925.

coccus meningitis, the specimens of fluid analyzed were obtained previous to serum therapy. In these fluids the sugar varied from 0 to 31 mg. and the lactic acid from 22.8 to 54.3 mg. per hundred cubic centimeters. Subject B. A. presents a spinal fluid sugar of 84 mg. with a lactic acid of 22.5 mg. after twenty-two days of intraspinal serum therapy and nine days before death. In the three following cases of pneumococcus and streptococcus meningitis, an increase in the lactic acid is noted with a drop in the sugar.

Eight of the eleven cases of tuberculous meningitis reported give figures for the sugar between 10 and 30 mg. per hundred cubic centimeters. Figures of 60, 68 and 75 mg. were obtained in the three remaining cases. Wilcox and Lyttle have noted high spinal fluid sugars in the early stages of tuberculous meningitis. It is probable that the hyperglycemia observed in tuberculosis may influence the spinal fluid sugar in the early stages of the meningitis. The lactic acid was found to vary

TABLE 6.—*Sugar and Lactic Acid of Spinal Fluid in Meningococcus Meningitis After Intraspinal Serum Therapy*

Patient	Date	Sugar, Mg. per 100 Cc.	Lactic Acid, Mg. per 100 Cc.	Remarks
M. F. ..... Aged 1 yr. 11 mo.	3/26/25	33	28.3	Before serum
	3/30/25	15	30.2	Before serum
	4/ 2/25	13	10.4	Serum given from March 30 to April 6 daily
	4/ 3/25	39	17.5	
	4/ 9/25	21	6.7	Discharged 10 days later
D. K. ..... Aged 5 mo.	11/17/25	42	37.2	Blood sugar = 166 mg.
	11/18/25	0	56.7	Blood carbon dioxide combining power = 47.5
	11/19/25	30	76.8	Spinal fluid carbon dioxide combining power = 35.2
	11/20/25	0	72.1	Deatn 2 days later

from 22.0 to 44.5 mg. per hundred cubic centimeters. There appears then no very marked difference in the concentration of the lactic acid of the spinal fluid in tuberculous compared with that in meningococcus meningitis.

The data recorded in table 6 demonstrate the relation of the variations of the sugar and lactic acid of the spinal fluid to the progress of the disease. Case M. F., in the first specimen of fluid analyzed, gave a sugar of 33 mg. and a lactic acid of 28.3 mg. per hundred cubic centimeters. After four days, during which no serum had been administered, the sugar dropped to 15 mg. and the lactic acid rose to 30.2 mg. Antimeningococcus serum was given intraspinally from March 30 to April 4, and during this period there was at first a decrease in the sugar to 13 mg., followed by a rise to 39 mg. The lactic acid showed a decrease to 10.4 mg. with a slight rise the following day to 17.5 mg. The relatively high spinal fluid sugar and lactic acid on April 3 are no doubt due to the fact that on this day the specimen of spinal fluid

was drawn about four hours after a meal containing cereal and milk. Goodwin and Shelley have shown that the ingestion of carbohydrate by mouth produces an increase in the spinal fluid sugar which reaches its maximum in about four hours and returns to normal in about six hours. Nishimura [4] and Katayama and Killian [16] have noted a rise in the blood lactic acid after carbohydrate taken by mouth. Data will be presented later in this communication to show that variations in the concentration of lactic acid in the blood are readily reflected in similar changes in the spinal fluid.

With the object of determining the relative diffusibility of the lactic acid into and from the cerebrospinal fluid, a comparison has been made of the sugar and lactic acid of both the spinal fluid and the blood. The specimens of blood and spinal fluid were obtained during the fasting and resting state and as close in time as possible. The sugar of the spinal fluid in the first two instances (table 7) forms 78 and 44 per cent, respectively, of the blood sugar, and the lactic acid 58 and 78 per cent of the blood lactic acid. A similar relation of the concentration of the sugar and lactic acid of the spinal fluid to their concentration in blood is seen in the following six cases, with the exception of M. H. (table 7). Here a slightly higher concentration is seen in the spinal fluid than in the blood. One of the three cases of encephalitis studied showed an abnormally high spinal fluid lactic acid although the sugar was not decreased. Again the spinal fluid withdrawn after the uremic convulsions in A. W. (table 7) has a high figure for the lactic acid, but this is less than the corresponding figure for the blood. Since in these two instances the spinal fluid sugar bears a normal ratio to the blood sugar, it is evident that this increased lactic acid in the spinal fluid cannot be derived from a fermentation of the sugar. The following subject (A. K., table 7) in the specimens removed shortly after admission when the temperature was 99 F. over a period of two days, showed a blood lactic acid of 19.6, and a spinal fluid lactic acid of 17.2 mg. per hundred cubic centimeters, and a normal ratio of sugar in the spinal fluid to that of the blood. However, ten days later when the temperature varied from 103 to 104 F., accompanied by leukocytosis and clinical evidence of a bilateral mastoiditis, the lactic acid rose in both the blood and the spinal fluid to 37.8 and 34.4 mg. per hundred cubic centimeters, respectively. The rise in lactic acid was accompanied by an increase in the sugar of 12 mg. in the blood and 17 mg. in the spinal fluid. At no time, however, did the spinal fluid show any bacteria or other evidence of a meningitis. In the two following cases (E. Z. and A. M., table 7), the meningitis was consequent to an acute infection,

16. Katayama, I., and Killian, J. A.: Proc. Soc. Exper. Biol. & Med. **23**:173, 1925.

and the bacteria were found in the spinal fluid. In these subjects hyperglycemias were noted, but there was an absence of sugar from the spinal fluid. The spinal fluid lactic acid was increased to about 200 per cent of the normal, but is below the figure for the blood lactic acid.

Hirsch has observed the development of transient hyperglycemia associated with a depression of the alkali reserve of the blood plasma following the intravenous injection of pathogenic bacteria into rabbits. He believes the increase in blood sugar may be due to the decrease of the normal alkali reserve of the plasma, since similar changes in blood sugar were noted after injections of sodium acid phosphate. However, subcutaneous administration of carbonate or bicarbonate solutions did

TABLE 7.—*Comparison of the Sugar and Lactic Acid of the Spinal Fluid and Blood*

	Blood		Spinal Fluid		
Patient	Sugar	Lactic Acid	Sugar	Lactic Acid	Remarks
E. A.	100	19.3	78	11.3	Normal
M. A.	79	14.4	35	11.3	Normal
M. H.	71	10.6	41	11.8	Glaucoma
S. W.	83	11.1	73	10.6	Glaucoma
J. B.	155	15.2	94	11.3	Brain tumor
I. S.	92	11.8	63	10.5	Chorioretinal optic nerve atrophy
S. T.	83	14.3	65	12.0	Clinical diagnosis: meningo-encephaltis (measles)
J. S.	96	18.0	72	14.0	Epidemic encephalitis
R. M.	100	8.5	72	7.7	Polioencephalitis
L. M.	112	26.5	68	23.2	Epidemic encephalitis
G. M.	87	28.5	68	26.5	Encephalitis
A. W.	161	27.0	103	22.3	After convulsions; chronic nephritis
A. K.	73	19.6	35	17.2	Otitis media, bilateral; temperature normal
	85	37.8	52	34.4	Ten days later; temperature 103-104 F.
E. Z.	161	27.7	0	23.4	Pneumonia, with pneumococcus meningitis
A. M.	143	29.1	0	27.9	Mastoiditis, meningitis streptococcus hemolyticus
B. A.	103	15.3	67	12.1	Epilepsy
	104	21.2	88	24.7	Twenty minutes after convulsions
R. N.	111	16.2	60	11.0	Epilepsy
	109	21.2	67	25.2	Twenty minutes after convulsions

not prevent the acidosis produced by the bacterial injections. The concentration of sugar in the blood seemed to be independent of the number of leukocytes. In the cases reported in the tables it is seen that acute infections are associated with hyperglycemia, and that corresponding to this rise in blood sugar there is an increase in the spinal fluid sugar in the absence of a meningitis. However, in the meningitic fluids the spinal fluid showed an absence of sugar in spite of the hyperglycemia.

We cannot here enter a discussion of the factors influencing the lactic acid content of the blood, beyond the statement that the development of an acute bacterial infection, associated with leukocytosis and increase in body temperature, provokes an increase in the concentration of lactic acid in the blood. This increased formation of the lactic acid may be a factor diminishing the alkali reserve of the blood plasma. It appears

from the data presented in table 7 that increases of this compound in the blood are accompanied by corresponding rises in the spinal fluid. The increase in the lactic acid of the spinal fluid in cases L. M., G. M. and A. W. cannot be accounted for by fermentation of the spinal fluid sugar, but must be derived from the high blood lactic acid. The fact that in all the cases reported, excluding those of epilepsy (table 7), there is a fairly constant relation of the concentration of lactic acid of the spinal fluid to that of the blood indicates that lactic acid must be readily diffusible. This ready diffusion of the lactic acid may account for the fact that in no instance do we find an amount of lactic acid in the spinal fluid corresponding to the sugar lost.

Another possible source of this increased lactic acid of the spinal fluid in meningitis may be the disintegration of leukocytes, since it has been observed in table 5 that the purulent meningitides show the highest figures for lactic acid. Ito's [17] observations on the lactic acid content of pus are of interest in this connection. The pus was obtained from the pleura by thoracocentesis or rib resection, and on this fresh material Ito found that *d*-lactic acid formed about 250 mg. per hundred grams, and that during autolysis for four days the increase in the acid amounted to about 10 per cent of the initial figure. Levene and Meyer [18] have shown that leukocytes suspended in Henderson's phosphate mixture containing glucose produced glycolysis with formation of lactic acid without evidence of oxidation. The observations made on the two subjects recorded in table 8 lend further evidence, we believe, to this explanation of the origin of the increased lactic acid in the purulent meningitides.

REPORT OF CASES

CASE 1.—C. B. was admitted to the hospital, December 10, with a tentative diagnosis of tuberculous meningitis, but tubercle bacilli were not found in the spinal fluid until December 13. In the meantime, following the removal of the spinal fluid, a corresponding volume of antimeningococcus serum was introduced intraspinally. In the first specimen of fluid obtained the sugar was found to be 21 mg. and the lactic acid 18.6 mg. per hundred cubic centimeters. The total cell count was 186 per cubic millimeter, and of these 58 per cent were lymphocytes. At this time the temperature was 98 F. Following the intraspinal serum therapy, the cell count rose, reaching its maximum the following day, and then diminished. Of the total cells counted on December 11 and 12, from 79 to 81 per cent were of the polymorphonuclear variety. From December 11 to 14, the temperature varied from 101 to 103 F. A count of the cells was not made in the specimens obtained after December 13. It is evident from the table that the period of intraspinal serum therapy is characterized by an increase in the lactic acid content of the spinal fluid. The maximum figure for the lactic acid was 26.2 mg. on December 14, twenty-four hours after the introduction of 50 cc. of serum. After

17. Ito, H.: J. Biol. Chem. **26**:173 (Aug.) 1916.

18. Levene, P. A., and Meyer, G. M.: J. Biol. Chem. **11**:361, 1912

the serum therapy was discontinued, the lactic acid returned to normal. There are marked variations in the sugar concentration of the spinal fluid; however, the fluctuations in the sugar do not appear to bear definite relation to the changes in lactic acid. It appeared possible that the increase in lactic acid after intraspinal serum therapy might be due to lactic acid contained in the serum. Triplicate analyses of the serum gave figures for sugar from 63 to 68 mg., and for lactic acid from 10 to 12 mg. per hundred cubic centimeters.

CASE 2.—S. T. On admission the clinical diagnosis was meningococcus meningitis, but the laboratory findings did not support it. January 10 the spinal fluid contained 73 mg. of sugar and 11.3 mg. of lactic acid per hundred cubic centimeters. Ten cells per cubic millimeter were seen. The following day blood and spinal fluid were obtained simultaneously; the results are recorded in table 7 (S. T.). A normal ratio was noted of the concentration of sugar and lactic acid

TABLE 8.—*Sugar and Lactic Acid of Spinal Fluid After Antimeningococcus Serum Intraspinally*

Patient	Date	Sugar, Mg. per 100 Cc.	Lactic Acid, Mg. per 100 Cc.	Leukocytes, per C.mm.	Serum, Cc.
C. B.	12/10/25	21	18.6	186	
Aged 1 year					20
Tuberculous meningitis	12/11/25 (a.m.)	53	21.5	3,400	
					10
	12/11/25 (p.m.)	31	25.9	836	
					10
	12/12/25	..	....	312	
					10
	12/13/25	17	19.8	187	
					50
	12/14/25	25	26.2	.....	
	12/15/25	43	19.4	.....	
	12/16/25	55	16.1	.....	
	12/18/25	25	8.6	.....	
	12/19/25 death				
S. T.	Jan. 10	73	11.3	10	
Aged 2 years					10
Clinical diagnosis: meningitis (?)	Jan. 11	65	11.9	724	
					25
	Jan. 12	57	29.5	4,200	
					25
	Jan. 13	60	34.0	4,000	
					25
	Jan. 14	..	....	1,600	
					15
	Jan. 15	117	37.9	7,400	
	Jan. 15 death				

of the spinal fluid to their concentration in the blood. During January 10 and 11 the temperature had been normal, but from January 12 to the time of death on January 15 it varied from 101 to 106 F. In this case serum therapy was continued until the day of death, and during this period there was a steady rise in the lactic acid from 11.9 to 37.9 mg. per hundred cubic centimeters. No significant change was observed in the spinal fluid sugar until two hours before death on January 15, when it rose to 117 mg. per hundred cubic centimeters. Following the intraspinal serum administrations, the cells counted in the spinal fluid were enormously increased, reaching a maximum of 7,400 on January 15. Of the total cells, polymorphonuclear leukocytes formed from 85 to 95 per cent.

In both cases reported in table 8 the rise in lactic acid of the spinal fluid does not appear as great as might be expected from the cellular metabolism indicated by the cell counts of the fluids. However, when

it is recalled that the lactic acid of the cerebrospinal fluid is carried off by the blood, producing similar changes in the concentration of this compound in the systemic blood, the significance of the figures becomes more striking. The amount of lactic acid produced does not appear to depend on the nature of the infecting organism; hence, determinations of the lactic acid of the spinal fluid in meningitis are of no value in ascertaining specific etiology. However, such studies add to our knowledge of changes in the body's metabolism during acute infections, and a rational therapy for such infections must consider the associated disordered metabolism.

SUMMARY

The lactic acid content of normal spinal fluid during the fasting and resting state varies from 6 to 10 mg. per hundred cubic centimeters. The lactic acid concentration of the spinal fluid bears a close relation to its concentration in the blood. An increase of the lactic acid of the blood is associated with a similar increase in the spinal fluid, and the reverse of this appears true.

An increase of the lactic acid of the spinal fluid and of the blood was found in nephritis and epilepsy following the convulsions. In epilepsy the spinal fluid after the convulsions gave figures for lactic acid exceeding those for the blood obtained at the same time.

Spinal fluids obtained from cases of meningitis showed high figures for lactic acid. The source of this increased formation of the lactic acid appears to be the cellular metabolism. In some instances no decrease was noted in the sugar in fluids in which the lactic acid was increased above normal; in others, however, no reaction for sugar was obtained. In no instance did the increase in lactic acid account for all the sugar lost.

YELLOW SPINAL FLUID ASSOCIATED WITH TUMOR OF THE BRAIN*

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Xanthochromic spinal fluid has been observed in association with numerous diseases. Busch,[1] in 1897, described a sarcoma filling the fourth ventricle, growing into the aqueduct and infiltrating the basal and spinal meninges. The ventricular fluid was yellow. Other early observers noted yellow spinal fluid, as a rule following apoplexy and trauma of the skull and in inflammatory conditions of the brain and cord. The conditions underlying the appearance of the pigment in yellow fluid have been rather extensively studied and as these conditions are pertinent to the subject of tumors of the brain, a brief review of the knowledge of them may not be out of place.

Lange [2] and Scully [3] have classified xanthochromic fluids according to the source of the pigment into three groups: (1) icteroid, (2) serogenic and (3) hemolytic. Those of the first group are dependent on a marked degree of jaundice and are without significance in the present study.

Xanthochromia of serous origin is caused by the addition of serum pigments, bilirubin and those of the carotinoid group. It is usually associated with obstruction and the formation of a cerebral or spinal culdesac isolated from the remainder of the spinal subarachnoid space. The obstruction may be of two kinds: compression such as is produced by a tumor of the cord, meninges or vertebrae; or adhesions of an inflammatory process. The first is associated with venous obstruction, the second with inflammatory congestion. Both conditions favor transudation of serum, with the addition of serum pigment to the cerebrospinal fluid. Cushing and Ayer [4] have shown that xanthochromia results above, as well as below, the site of the lesion. Cushing attributes the fluid changes both above and below the block to direct transudation into the

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* Read before the Society of Neurological Surgeons, Rochester, Minn., Nov. 7, 1925.

1. Busch, C.: Ein Fall von ausgebreiter Sarkomatose der weichen Häute des centralen Nervensystems, Deutsche Ztschr. f. Nervenh. **9**:114-118, 1897.

2. Lange, C.: Was leistet die reine Liquordiagnostik bei der Diagnose der Hirntumors? Mitt. a. d. Grenzgeb. d. Med. u. Chir. **33**:582-610, 1921.

3. Scully, F. J.: Yellow Spinal Fluid, Its Origin and Significance, Arch. Neurol. & Psychiat. **10**:83-99 (July) 1923.

4. Cushing, Harvey; and Ayer, J. B.: Xanthochromia and Increased Protein in the Spinal Fluid Above Tumors of the Cauda Equina, Arch. Neurol. & Psychiat. **10**:167-193 (Aug.) 1923.

fluid from the surface of the tumor itself, and believes that all tumors that are subarachnoid and are bathed by the cerebrospinal fluid (the acoustic tumors, for example) are accompanied by some degree of xanthochromia although it may not be detected in fluids remote from the situation of the tumor. Ayer, and probably most other observers, believe that the transudation takes place from engorged vessels. Blocking of the normal channel of exit concentrates the products of transudation below the lesion; above the lesion, the abnormal constituents are diluted and removed by the normal circulation of the fluid. This explains the difference in the concentration of pigments and protein above and below the block.

Xanthochromia of hemolytic origin is associated with bleeding into the subarachnoid space. The pigment arises from two sources: the serum and the erythrocytes. Besides the serum pigments, hemoglobin derived from the disintegration of erythrocytes is present. According to Leschke,[5] the latter substance is reduced through intermediate stages to bilirubin. Of the two sources of pigment, the cellular one provides the distinguishing feature. The presence of erythrocytes, a positive benzidine or guaiac test, or absorption spectra of hemoglobin and its derivatives at once places the yellow fluid, at least partly, in the hemolytic group.

Lange [2] has considered at length the fluid changes following bleeding. Immediately after hemorrhage has occurred the erythrocytes can be centrifugalized, a clear supernatant fluid being left. About the eighth day the supernatant fluid will present a red to yellow color detectable by the naked eye. The older the hemorrhage, the more completely the erythrocytes have been destroyed and the hemoglobin changed to a yellow, more easily dialyzable substance. From ten to twenty days after hemorrhage the fluid is yellow and shows a red sediment after centrifugalization. Old hemorrhage or repeated capillary hemorrhage will leave behind a light yellow fluid containing no erythrocytes or recognizable cellular pigment. The distinction between gross and capillary hemorrhage made by Lange is definite: if the hemorrhage is so small that no erythrocytes or cellular pigment can be found in the fluid, it is then capillary. Obviously such a yellow fluid cannot be distinguished from one of serous origin.

THE FREQUENCY OF THE OCCURRENCE OF XANTHOCHROMIA

Very few data concerning the frequency of yellow spinal fluid in cases of tumor of the brain are available. Vincent [6] found yellow fluid

5. Leschke, von Erich: Ueber die Gelbfärbung (Xanthochromie) der Zerebrospinalflüssigkeit, Deutsche med. Wchnschr. **47**:376-377 (April 7) 1921.

6. Vincent, C.: Informateur d. alién. et d. neurol. **5**:147, 1912, quoted by Greenfield, J. G.: On the Value of a Quantitative Albumin Estimation of the Cerebrospinal Fluid, with Special Reference to the Syndrome of Massive Coagulation and Xanthochromia, Lancet **2**:685-688, 1912.

in several cases of tumor of the cerebellopontile angle. Quincke [7] mentions the occurrence of one yellow fluid in a series of forty-five cases of brain tumor. Horrax [8] remarks that he has seen a number of examples in cases of brain tumor. Leschke reported from the literature seven, and Scully fourteen cases of cerebral neoplasm associated with this phenomenon. These observations would seem to indicate that xanthochromia is rather infrequent in brain tumor. But Lange asserts that xanthochromia is an almost constant finding in brain tumor. He gives no statistical data. The present study indicates comparatively frequent occurrence of yellow fluid in brain tumor.

Two groups of consecutive cases of tumor of the brain in which spinal puncture had been performed were reviewed. Group 1 included twenty-five cases in which no operation was performed; five (20 per cent) yielded yellow fluid. The diagnosis in five was verified at necropsy, and in four of these the fluid was colorless; in one it was xanthochromic. In group 2 there were forty-eight cases in which operation was performed; in all, the history, the neurologic or the operative findings left no reasonable doubt concerning the accuracy of the diagnosis. Ten (20.8 per cent) of the fluids were xanthochromic. The presence of a tumor was verified by necropsy or operative procedures in thirty-five of the cases in this group; nine (25.7 per cent) of these had yellow fluid.

CASES AVAILABLE FOR ANALYSIS

These findings suggest that insufficient attention has been directed to the origin of xanthochromia, and of the bearing of the sign on diagnosis, prognosis and localization in cases of brain tumor. Available cases in the literature have been analyzed with this end in view.

In the ten cases of brain tumor with yellow spinal fluid reported by Erb,[9] Horrax,[8] Sprunt and Walker,[10] Reich [11] and Greenfield,[12] the lesion was located at necropsy. The reports of the type of tumor and findings in the spinal fluid are satisfactory in six. The essential facts

7. Quincke, H.: Zur Pathologie der Meningen, Deutsche Ztschr. f. Nervenh. **40**:78-130, 1910.

8. Horrax, Gilbert: Studies on the Pineal Gland, Arch. Int. Med. **17**:627-645 (May) 1916.

9. Erb, Wilhelm: Ueber die Diagnose und Frühdiagnose der syphilogenen Erkrankungen des zentralen Nervensystems, Deutsche Ztschr. f. Nervenh. **33**: 425-449, 1907.

10. Sprunt, T. P., and Walker, J. E.: The Significance of Xanthochromia of the Cerebrospinal Fluid, Bull. Johns Hopkins Hosp. **28**:80-86 (Feb.) 1917.

11. Reich, Joseph: Ueber Gelbfärbung der Cerebrospinalflüssigkeit, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **25**:721-733, 1913.

12. Greenfield, J. G.: On Froin's Syndrome, and Its Relation to Allied Conditions in the Cerebrospinal Fluid, J. Neurol. & Psychopath. **2**:105-141 (Aug.) 1921.

of these cases are presented in table 1. Several cases of diffuse sarcomatosis of the meninges are not included because the involvement of the spinal theca introduces the factor of obstruction with stasis in this situation.

Xanthochromic fluid was encountered in fifteen cases of our series. Six are eliminated from consideration: five, because the diagnosis was

TABLE 1.—*Cases of Brain Tumor Associated with Xanthochromic Spinal Fluid*

Author	Nature and Site of Tumor	Color	Albumin, per Cent	Nonne Reaction	Noguchi Reaction	Lymphocytes, c.mm.	Polymorphonuclears, c.mm.	Blood Elements
Sprunt and Walker	Endothelioma, left middle fossa	Lemon	....	..	..	4	....	Few old erythrocytes
		Lemon	....	..	..	4		
Horrax....	Pineal struma embedded in a hemorrhagic mass (implant in third ventricle)	Straw	....	+	+	85	....	1,011 old erythrocytes
		Yellow*	....	..	..	17	....	561 old erythrocytes
Erb.....	Vascular glioma of right cerebral peduncle	Clear	....	..	..	Many	....	
		Amber	....	..	..	Many	Many	Many erythrocytes
		Amber	....	..	..	Many	Many	Many erythrocytes
Reich..... (case 1)	Vascular sarcoma involving both frontal lobes, corpus callosum and septum pellucidum	Amber	....	..	..	....	Many	Crystals and structureless elements
		Yellow	0.07	+	..	++	Many	
		Yellow	0.06	+	..	+++		
Reich..... (case 2)	Cystic glioma of corpus callosum	Yellow	....	..	..	Many	Many	Erythrocytes and crystals
Reich..... (case 3)	Carcinoma (primary in bronchus) of basilar membranes filling right lateral ventricle; many new and old capillary hemorrhages	Light yellow	....	+	..	Few	....	Crystals
Greenfield (case 1)	Gumma involving left basal ganglia and walls of ventricles	Yellowish	0.06	..	..	10	..	
Greenfield (case 2)	Glioma of left cerebral hemisphere extending into lateral ventricle	Yellowish	0.045	+	..	21	..	
Greenfield (case 3)	Carcinoma (primary in stomach) involving tentorium cerebelli, cerebellum and temporal lobe	Pale yellow	0.06	+	..	..	..	
Greenfield (case 4)	Glioma involving right thalamus, right corpus mamillare and anterior fornix	Slightly yellowish green	0.18	+++	..	12	..	

* Ventricular puncture.

not substantiated by operative or postmortem examination; one, because spinal puncture having been performed two weeks prior to the date of registration at the clinic, the possibility of a traumatic origin of the xanthochromia could not be eliminated. That this possibility must be considered in the estimation of the significance of xanthochromic fluid is obvious. Five cases in which the tumors were sufficiently localized to be of suggestive value are incorporated in table 2. Four cases in

which the tumor was exactly localized by operation or postmortem examination are presented in table 3.

THE SOURCE OF THE PIGMENT

Most observers, including Reich,[11] Reichmann,[13] Scully,[3] Sprunt and Walker,[10] Lange[2] and Leschke[5] consider capillary hemorrhage the source of xanthochromia associated with tumor of the brain. Cushing[4] alone has indicated a belief in a serous origin. The presence of the erythrocytes or blood crystals in the fluids in the cases of Sprunt and Walker[10] Horrax,[8] Erb[9] and Reich,[11] and in my cases 4 and 5 (table 2),

TABLE 2.—*Cases of Incompletely Localized Tumor of the Brain Associated with Xanthochromic Spinal Fluid*

Case	Clinical Localization	Operative Findings	Spinal Fluid: Color	Nonne Reaction	Erythrocytes, c.mm.	Lymphocytes, c.mm.	Polymorphonuclears, c.mm.
1	Right frontomotor area or third ventricle	Right midfrontal convolution flattened; mass 4 cm. below surface; ventricle collapsed	Faint yellow	..	..	..	..
2	Suprasellar.....	Ventriculogram: mass blocking foramen of Monroe, probably in median line	Yellow tinge	+	..	1	..
3	Cerebellar.....	Thick yellow gelatinous material from a large subcortical neoplasm (2 cm. in diameter) of the right lobe of the cerebellum and the vermis	Yellow	+	..	4	Occasional
4	Left uncus and wall of inferior horn of lateral ventricle	Left temporosphenoidal mass 3 cm. below surface	Yellow 2+	+	Few	2	..
5	Frontal lobe.....	Ventriculogram: bloody fluid from each lateral ventricle; tumor compressing wall of left lateral ventricle	Light yellow	+	..	13	9
			Light yellow	..	Occasional	25	9

as well as in cases 1, 3 and 4 (table 3), support the contention of this group of observers, that the xanthochromia is of hemolytic origin. The xanthochromic fluids in cases 1, 2 and 3 (table 2), and in case 2 (table 3), contained no cellular elements. Unfortunately no tests for the presence of hemoglobin were performed. These cases, therefore, cannot be placed in the hemolytic group. Had such tests been performed, with negative results, the classification of the cases would have been rendered no less difficult, because of the ultimate reduction of hemoglobin to bilirubin. That the source of the xanthochromia, when the fluid

13. Reichmann, V.: Ueber einen operativ geheilten Fall von mehrfachen Rückenmarksgeschwülsten bei Recklinghausenscher Krankheit nebst Bemerkungen über das chemische und cytologische Verhalten des Liquor cerebrospinalis bei Gehirn- und Rückenmarksgeschwülsten, Deutsche Ztschr. f. Nervenh. **44**:95-110, 1912.

contains bilirubin alone, is a hemolytic one can be established only when the concentration of bilirubin rises above that present in the blood stream. Because of the physical principle underlying transudation, these substances in a xanthochromic fluid of serous origin can only attain, not surpass, this percentage. Experimental work is in progress to determine the practical value of these theoretic considerations and to establish, if possible, the fact of a serous origin for xanthochromic fluid associated with tumor of the brain.

FACTORS UNDERLYING THE PRODUCTION OF XANTHOCHROMIA

Obviously, to produce xanthochromic fluid of either hemolytic or serous origin, the tumor must be so situated that its surface is in contact with the cerebrospinal fluid. Reich first considered this relationship to be essential from a study of his three cases, all of which were investigated at necropsy. The fourteen localized tumors of our series avail-

TABLE 3.—*Cases of Localized Tumor of the Brain Associated with Xanthochromic Spinal Fluid*

		Spinal Fluid			
Case	Nature and Site of Tumor	Color	Nonne Reaction	Lymphocytes, c.mm.	Erythrocytes, c.mm.
1	Large, vascular neurocytoma of left frontal lobe, involving wall of lateral ventricle, with rupture and hemorrhage into ventricles; implants in left lateral and fourth ventricles	Yellow	+	1	Many
2	Dark red encapsulated endothelioma (4.5 by 4 by 3 cm.) covered with many blood vessels	Pale yellow	+	1	..
3	Pulpy reddish-purple tumor involving sphenoid and frontal lobes superior and anterior to chiasma	Faint yellow	+	1	Numerous
4	Carcinomatous (primary in lung) meningo-encephalitis	Yellow Light straw	+ +	11 7	Few Few

able for study involved either the ventricular or the external surface of the brain, and support Reich's contention that this is the condition sine qua non for the production of xanthochromia. Further, although only partially satisfactory confirmation is to be found in the findings in the cases presented in table 2, there is strong presumption of involvement of the ventricular wall. The location of the tumors in four cases in group 1 and six in group 2, all associated with colorless spinal fluid, was studied at necropsy. The freedom from involvement of the ventricular wall or external surface emphasized the need of this factor for the production of xanthochromia.

Nine cases of tumor involving the ventricular or external surface of the brain are presented in table 4. Each was associated with colorless fluid. Obviously an additional factor is necessary for the production of xanthochromia.

A review of the descriptions of the macroscopic and, when available, histologic picture of both the tumors of this group and those associated

with yellow spinal fluid reveals interesting facts. The vascularity of four of the fourteen tumors (tables 1 and 3) associated with xanthochromic fluid is not mentioned. Nine of the ten remaining tumors are described as being vascular. Reich's case 2 is the exception. It may be said that tumors associated with yellow fluid are usually vascular and, hence, that a yellow fluid in all probability indicates a vascular tumor.

Of the nine tumors of table 4, three are avascular, and six are probably vascular. Obviously, the two factors, surface involvement and vascularity, while necessary to the production of xanthochromia, do not insure its presence.

Any tumor of firm consistency, encapsulated or not encapsulated, usually possesses well formed blood vessel walls supported by stroma adequate to prevent rupture and hemorrhage. Soft encapsulated tumors may bleed within themselves; their capsules prevent the escape of blood to the surrounding structures. Soft nonencapsulated tumors, on the

TABLE 4.—*Brain Tumor Involving the Cortical or Ventricular Surfaces Associated with Colorless Fluid*

Case	Description of Tumor
1	Necropsy: firm, yellowish white, rounded, smooth surfaced tumor of the third ventricle (8 by 6 by 6.5 cm.) composed of interlacing strands of broad collagen-like fibers, acellular; walls of blood vessels well formed
2	Purplish-red, fairly firm suprachiasmal tumor
3	Reddish-blue encapsulated mass resting on chiasma
4	Vascular purplish-red encapsulated left parasagittal endothelioma (6 by 5.5 by 5 cm.)
5	Dark purplish-red encapsulated endothelioma surrounded by large veins (6 by 5 by 5 cm.)
6	Encapsulated right frontomotor malignant endothelioma (8 by 7 by 6 cm.) associated with marked vascularity; weight, 155 Gm.
7	Acoustic tumor
8	Acoustic tumor
9	Left temporoparietal mass of very large tortuous vessels

contrary, whether the vessel walls are strong or not, contain inadequate supporting stroma, and are prone to bleed. These are fairly dependable considerations of general pathologic anatomy. All brain tumors associated with yellow spinal fluid available for study in this series, with the exception of the endotheliomas and Reich's case 2, are nonencapsulated, vascular and of a consistency that can be described as soft. On the contrary, six tumors of table 4 (omitting the endotheliomas and the hemangioma from consideration at present), associated with colorless spinal fluid, are firm; three are encapsulated and avascular. The contrast between the structure and findings in the spinal fluid in the two groups of cases suggests that the foregoing general pathologic considerations bearing on the relationship of consistency and encapsulation on the one hand, and vascularity and proneness to hemorrhage on the other, apply as well to tumors of the brain as to tumors elsewhere in the body. This relationship of consistency and vascularity to hemorrhage is nicely illustrated in cases 2 and 3, table 4; both tumors were

firm but vascular (to judge from the external appearance), yet neither produced xanthochromia of the spinal fluid.

The endotheliomas do not conform to the characteristics of the preceding group. In the four cases encountered in the present reported series, the presence of the encapsulation and firm consistency directs attention to the engorged blood vessels surrounding the tumor as the possible source of the xanthochromia in the case of Sprunt and Walker, and case 2, table 3. The engorged vessels and the free, fluid-bathed surfaces provide both accepted pathways for a serous origin of the pigment. On the contrary, if it is assumed that the erythrocytes in the second specimen of spinal fluid in the case of Sprunt and Walker (obtained only one week after the first) were not of traumatic origin, this spinal fluid may be placed in the hemolytic group. The spinal fluid in case 2, table 2, is indeterminate. Further observations must be recorded before definite conclusions can be drawn concerning the source of the xanthochromia in the cases of endothelioma.

Of the four endotheliomas described here, all were surrounded by engorged vessels. One only was accompanied by a yellow spinal fluid. Whatever the source of the pigment, if the pericapsular vascularity be the only factor, xanthochromic spinal fluid should be expected not only with the other three endotheliomas, but with the hemangioma (table 4) as well. However, no significant deductions to account for its presence in this case can be drawn from the site of the tumor, the duration of symptoms or the degree of intracranial pressure present.

THE SIGNIFICANCE OF XANTHOCHROMIA ASSOCIATED WITH TUMOR OF THE BRAIN

The production of xanthochromia, therefore, depends on four factors: (1) the involvement of the ventricular or external surface, (2) the state of encapsulation, (3) a certain minimal degree of softness and (4) the presence of vascularity. Conversely, xanthochromic spinal fluid associated with tumor of the brain must be interpreted to mean that the tumor involves the external or ventricular surface and that the tumor, if not encapsulated, is softer and more vascular than the usual neoplasm or, if encapsulated, is surrounded by a plexus of engorged vessels.

At least the majority of the xanthochromic spinal fluids associated with brain tumor are hemolytic in origin. The hemorrhages on which their appearance depends are conceived of as being scanty and recurrent. That the factors mentioned will determine the chances of transudation from tumors may well be believed. It is a reasonable assumption that the softer and more vascular a tumor is, the more likely that transudation as well as hemorrhage will occur. Tumors which bleed

probably permit transudation as well. While it cannot be denied that all tumors bathed by the cerebrospinal fluid are accompanied by some degree of xanthochromia, as Cushing believes, the possibility is that at least those which are soft and vascular, or encapsulated but surrounded by engorged vessels, produce by transudation some degree of xanthochromia, recognizable or not, in the fluid drawn from the lower end of the spinal theca.

In nonencapsulated tumors, the first two factors being fixed quantities, the size and briskness of the hemorrhages, and consequently the number of erythrocytes and the concentration of cellular pigments in the spinal fluid, will vary directly with the degree of vascularity and softness of the tumor. Xanthochromic fluid, containing many erythrocytes, points to the presence of a more vascular and a softer tumor, more prone to bleed than one containing none or comparatively few erythrocytes.

Any procedure leading to marked reduction of the intracranial, and more particularly of the intraventricular, pressure would tend to disturb the shape and relative situation of a soft tumor involving the ventricular wall, cause distortion of its internal structure and rupture of its vessels, and permit hemorrhage into its substance and into the ventricle itself. Such an accident in the course of operative procedures is an infrequent but none too happy experience of the surgeon. Death in case 1, table 3, resulted from hemorrhage into the ventricle from the tumor, probably incident to the reduction of intraventricular pressure. The tumor in this, as well as in other cases in which this has occurred, was very soft and vascular. If spinal puncture were performed, the fluids would in all probability be yellow and contain numerous erythrocytes, as did the fluid in case 1, table 3. Such a fluid should emphasize the danger of such an accident, increase the operative risk and possibly contraindicate any operative procedure leading to marked reduction in the intraventricular pressure.

CONCLUSIONS

1. The present review has led to the belief that a definite localizing and prognostic significance is attached to the presence of xanthochromic fluids in cases of brain tumor, and that the following conclusions, although based on the study of a comparatively small group of cases, are justified.

2. Yellow spinal fluid associated with tumor of the brain occurs much more frequently than the reported cases indicate. In the present series, xanthochromia occurred in approximately 20 per cent of the cases of tumor of the brain.

3. Xanthochromic spinal fluid associated with a tumor of the brain indicates the involvement of the ventricle or external surface of the brain, and that the tumor is sufficiently vascular and soft, or so sur-

rounded by engorged vessels, as to permit hemorrhage or transudation into the cerebrospinal fluid.

4. The available evidence points to a hemolytic origin for the xanthochromia accompanying tumor of the brain; a serous origin, while theoretically possible, has not been proved.

5. The hemorrhages accounting for the coloration are conceived of as being scanty and repeated.

6. The number of erythrocytes present is a measure of the softness and the vascularity of the tumor.

7. Xanthochromia combined with the presence of many erythrocytes, indicating the presence of a soft vascular tumor prone to hemorrhage, should greatly increase the risk of, and possibly contraindicate, those operative procedures which markedly reduce the intraventricular pressure.

Clinical and Occasional Notes

FIXATION OF THE CELLS OF THE CEREBROSPINAL FLUID WITH IODINE VAPOR*

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To obtain well preserved, well stained samples of cells of the spinal fluid would seem a simple feat. In fact, only through the development of a very laborious technic have workers in the past achieved success. The difficulty has been that if a drop of spinal fluid is placed on a slide and allowed to dry in air, so much shrinkage of the cells occurs, and so much deterioration, that sharp staining and exact differentiating are quite impossible. Acceleration of the drying with heat causes even worse alteration than drying at room temperature. Nor can a fluid fixative be added for fear of washing away the freely floating cells.

Alzheimer overcame these difficulties by adding to several cubic centimeters of fluid a large volume of alcohol, centrifugalizing it until a coagulum formed at the bottom of the tube, embedding the coagulum in celloidin and cutting sections. This elaborate technic sometimes yields beautiful preparations. But there are obvious technical and theoretical objections to it.

Vapor of osmic acid and vapor of iodine have been used for the fixation of delicate tissues by many workers. Most recently, Lewis[1] has used iodine vapor to fix tissue cultures. The nuclei and any phagocytic inclusions take a deep brown stain and the cytoplasm a lighter brown, allowing a contrast adequate for photography. His work suggested to us the use of iodine for the cells of the fluid; and it was found that drops of spinal fluid allowed to dry in an atmosphere of iodine vapor contain perfectly preserved cells.

METHOD

A strip of thick plate-glass is placed in a petri dish, and a few crystals of iodine are scattered over the bottom of the dish. Very gentle warming soon fills the dish with purple fumes. The slide or cover-slip, with a drop of fluid on it, is then placed in the dish and rested on the strip of plate-glass, and the cover replaced. Within a few moments the drop of fluid turns a light yellow brown, the cells becoming well fixed almost at once, long before the drop as a whole has dried. (If the process is watched in a hanging-drop preparation, with a single crystal of iodine in the bottom of the hollow-ground slide, the staining of the cells by the iodine can be seen to occur with great rapidity.)

The drop is kept in the iodine chamber until dry, in order to fix the cells firmly to the slide or cover-slip. At this stage the preparation looks very unpromising. It is a dirty purple, with minute crystals of iodine sublimated on it, and a film of coagulated proteins overlying all. The iodine can be completely removed, however, by washing the preparation for a few moments in a fresh, concentrated, aqueous solution of potassium iodide. It is important

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1. Lewis, W. H.: Endothelium in Tissue Cultures, Am. J. Anat. **30**:39 (Jan.) 1922.

to do this thoroughly, as the presence of residual iodine affects the staining; but one or two changes are always adequate. The potassium iodide is rinsed off with distilled water, and the preparation then is stained as desired.

The fixation thus secured is excellent. Even very fragile cells, such as swollen phagocytes in the height of activity, with great foamy cytoplasm, are perfectly preserved. And lymphocytes, which by ordinary methods invariably appear to have round dense nuclei, show with this fixation as great a range of nuclear shapes as they do in the living.

The exact temperature used does not seem to make any great difference, although too high temperatures are unnecessary and inadvisable. Our routine was to place the petri dish in a corner of the warm box in which we were making simultaneous studies of the living cells at body heat.[2] This temperature obviously could not damage the cells directly, and was warm enough to give an adequate concentration of the iodine vapor.

We have secured our best staining with the orthodox Unna-Pappenheim combination of pyronin and methyl-green. Sometimes it is best to reduce the methyl-green and increase the pyronin. It has also been found well to differentiate in absolute alcohol to which a little hydroquinone is added. Mayer's carmalum gives excellent stains after the iodine; but the blood-stains (Wright's or Wilson's) do not give very satisfactory results. We believe this to be due largely, however, to the changes that seem to occur in blood cells when they are thrown out into the fluid. In these studies of the living cells from spinal fluid we have found unmistakable evidence that the fluid is an abnormal environment for granulocytes and that they show definite changes when introduced into it.

The study of fluids in which there are few cells is greatly facilitated by this technic. The drop can be made as large as desired, and on a well cleaned cover-slip is held within a small area by its own surface tension. All the cells from a large drop will then settle down on a very small spot on the glass; and frequently a colored ring marks the outlines of this spot after staining, so that the field can be found with great ease and it is not necessary to move over the entire cover-slip in one's search for cells. In collecting the sample for examination it is, therefore, inadvisable to allow a large drop from the puncture needle to splash directly on the cover-slip. We use a small glass tube drawn to a point and sterilized, allowing the fluid to run into the tubing by applying its tip to the puncture needle. The size and concentration of the drop can then be easily controlled when it is transferred to the cover-slip.

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2. Kubie, L. S., and Shultz, G. M.: Vital and Supravital Studies of the Cells of the Cerebrospinal Fluid and of the Meninges in Cats, Bull. Johns Hopkins Hosp. **37**:91 (Aug.) 1925.

SPECIAL ARTICLE

NEUROPATHOLOGY

LECTURE NOTES *

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Neuropathology, like its sister subject, general pathology, often suffers from the misconception that its field is limited to the histopathologic changes observed with the microscope, and while this is one of its functions and a very important one, it by no means covers the field. In the broader view, it must include the histopathology of the nervous structures, but to permit of interpretation of the results of structural defects and destructive lesions in the brain and cord it must also take cognizance of their anatomic locus, their physiologic action and their phylogenetic relations.

Evolution has developed in the human nervous system receptive mechanisms attuned to respond selectively to restricted groups of physical stimuli, and we are naturally inclined to classify our environment according to these somewhat limited sensory capacities: vision, audition, etc. This anthropomorphic view, however, does not accord with our physical knowledge of the forms of energy available as possible stimuli. Our sensations represent only the final developmental result in man, and moreover only those in which sensory receptors have been developed in connection with certain higher sensory mechanisms which we designate as consciousness. For a broader view of our problems we must envisage man's *conscious* sensory equipment as restricted to the reception of a limited part of available physical stimuli and must accede that many organisms may respond to a very different range than does man. That this is true in the vegetable kingdom is obvious when we consider the responses of plants to photochemical stimuli—a group to which man is insensitive as far as conscious reception is concerned. The inflammatory reaction to sunburn, however, and the pigmentary deposits in tanning give evidence that man's body cells have not lost their responsiveness to this group of rays, although no nervous mechanism has survived for their especial reception. That other animals as well as the plants may have different capacities in this regard is indicated, however, by experiments which show that the honey bee reacts to ultraviolet light of a wave length outside of that part of the spectrum which

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is visible to man. The noise of the bat is so high pitched as to be near the limit of auditory reception in man—beyond that of many persons—and there is reason to believe that many insects generate and receive vibratory impulses beyond the human range of audible pitch frequencies. If we also consider differences in acuity of sense perception, the olfactory capacities of the osmatic animals will serve to emphasize further these varying responses of the phyla to restricted groups of environmental influences.

PHYSICAL FORCES AS NERVOUS SYSTEM STIMULI

Reviewing the fields of physical forces which might serve as stimuli, we may coarsely divide them into the following groups: (1) Radiations including heat and light; (2) energetics which may be further subdivided into (*a*) kinetic forces, (*b*) potential or gravitational forces; (3) chemical, and (4) electrical.

In his discussions of the special refinement of the receptors of the head end segments of axially arranged animals, Sherrington has called attention to the development in the leading segments of "glorified" receptors with much greater acuity though often with narrowed range of reception. Thus he speaks of the retina as a glorified warm spot, the cochlea as a glorified touch spot, etc. From this we might expect to find a specialized head ganglion or mechanism for each group of stimuli and a more diffuse somatic representation for the same group. Analyzing our groups in this way, we find:

1. Radiational.
   - (*a*) Heat reception by diffusely scattered receptors over the whole exterior of the body.
   - (*b*) Light reception concentrated in a group of receptors within the retina (vision).

2, *A*. Kinetic Energetics.
   - (*a*) Contact and low rates of vibration received by receptors scattered all over the body surface.
   - (*b*) Specialized reception of great acuity for the "touch" of alternating waves of condensation and rarefaction of the air by the cochlea (audition).

2, *B*. Potential Energetics.
   - (*a*) Gravitational effects as represented in the kinesthetic systems of muscles, joints, tendons, etc.
   - (*b*) Specialization in the vestibular apparatus to subserve the same adjustment to gravity.

3. Chemical.
   - (*a*) Chemoceptors in wide distribution throughout the gastro-intestinal tract, as, for example, those governing the pyloric reflex.
   - (*b*) Specialized chemoceptors of smell and taste.

Our fourth heading, "Electrical," finds no corresponding mechanism in our senses. It is obvious that electrical currents as such are not

among the commonly encountered natural forces to which living matter has had to adapt itself in its evolution. We should also note that electrical currents of proper intensity seem to be the only physical stimuli to which all nerve paths are equally responsive. This fact is of especial interest when we consider the modern views of nervous energy as an electrochemical force. One other point of interest is that in this list

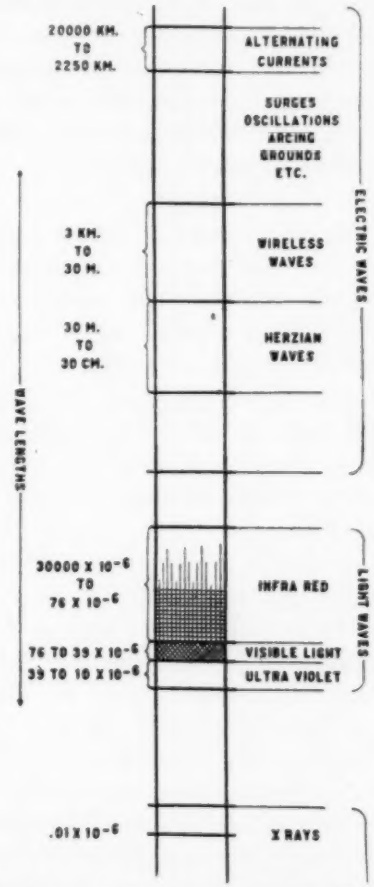

Fig. 1.—Chart showing extremely small group (lined and cross-hatched) of radiational stimuli directly accessible to the human sensory equipment. (Modified from Steinmetz.)

of external forces we have included no source of energy which is related to the sense of pain. Any stimulus over any sensory path if of more than physiologic intensity apparently induces pain. Pain is obviously a mechanism of warning that damage threatens or has been done to the organism itself and is in a different category than those sensory impressions which serve to inform the organism concerning its environment.

Figure 1, modified from Steinmetz to show graphically the extremely small range (cross hatched) of radiations which are immediately accessible to us as sensations without transmutation by the photographic plate, the fluorescent screen or some other interpreting device, will serve to emphasize the incompleteness of our sensory equipment.

While the range of radiations visible to the eye is extremely narrow (from 76 by 10^{-6} to 39 by $10,^{-6}$ or, as Steinmetz expresses it, less than one octave out of 60), an extremely acute perception has developed within this range not only for total volume of energy but also for differentiation between wave lengths as suggested by studies of the "just perceptible" differences in color which correspond closely to the actual number of wave lengths in the visible spectrum.

In connection with each group of the sensory receptors a central nervous mechanism has developed for the reception, recognition and recording of sensory data, and this emphasizes at once that the brain must be considered not as a single organ, as we do the liver, but as a complex group of specialized organs associated with each other by intimate anatomic and physiologic interrelations.

In the organs of the trunk a relatively few histologic samples will suffice to give a fairly accurate idea of the structural integrity of the organ as a whole. In the brain, on the other hand, not only must samples be taken from many areas, but they must be so handled during embedding and other technical steps that their exact anatomic source can be identified in the finished section. Common practice in the necropsy room, except when neuropathologic investigation is under way, consists in a gross examination of the brain with the removal of a single sample for histologic study. Often this is taken from the vertex in the frontal fields, sometimes from the temporal pole and sometimes from the occipital areas. Such haphazard sampling will, of course, serve in processes, the expression of which is generally diffuse, as for example simple chromatolysis or widespread meningitis. In most conditions it is misleading, and this is true not only for conditions with a selective attack but also for many moderately diffuse processes. In general paralysis, for example, diagnosis would be impossible from a single section taken from the occipital pole in many typical cases, or in the rarer form of Lissauer's general paralysis sections from the frontal zone would be of little value. Moreover, as Alzheimer has stated, the general paralytic process is not to be diagnosed by the histologic change in any one area, but the widespread distribution of the process over considerable surface is as characteristic as is the type of infiltration. It was the failure to recognize the importance of this factor that led Dr. Southard to characterize the general pathologist as a "man trained for the very careful study of all the organs of the body except the most important."

WIDESPREAD EFFECT OF LESIONS OF NERVOUS SYSTEM

It is obvious that the anatomic locus of a lesion is of paramount importance in determining its result. It is even of greater importance than etiology in many instances. Lesions dependent on the same etiologic factor but occurring in two different brain fields will give entirely different clinical pictures; for example, vascular obliteration leading to hemianopia in the calcarine area or to hemiplegia in the internal capsule. On the other hand, two very different etiologic moments acting on the same anatomic area may give the same clinical picture, for example, the destructive infiltration by a brain tumor and a destructive vascular lesion in the motor area, both resulting in a cortical paralysis.

Another factor enters when we consider the effect of certain lesions on the physiologic action of a given locus. Lesions with the same etiology and involving the same locus may in two persons give diametrically opposed clinical symptoms. Thus a gumma over the motor area may initiate overdischarge resulting in convulsions or in weakened discharge resulting in general paralysis or paralysis of voluntary motion. We therefore speak of discharging and destructive lesions.

Because of these results, we must consider not only the etiologic factor but also its anatomic locus combined with the influence which such a lesion may have on that particular center. In many instances diagnosis may be said to rest largely on evidence obtained from other channels than the study of the nervous symptoms. This is especially true in the psychoses and in syphilis of the brain. The age of the patient, the condition of the arteries, a history of alcoholism, recent infections or of familial diseases and laboratory examinations, especially in syphilis, nephritis and the thyroid toxemias, are all examples of data of importance to the clinician often equal in their value in determining etiology to the specific brain or cord symptoms.

Another factor of importance is that in few lesions of any size is the result limited to the immediate locus because of involvement of parts of more distant neurons coursing past the damaged locus as association or projection tracts. This point is emphasized by von Monakow in his explanation of the association of word-blindness with hemianopia.

We are coming to appreciate more and more clearly in all fields of medicine that a lesion of one organ not only will result in its own symptomatic expression of disorder but may also interfere with the function of other organs. The familiar vicious circle of chronic nephritis, arteriosclerosis and myocarditis is an example, and evidence, though as yet hazy and poorly understood, is being obtained in the field of the endocrine system. Experimental hypophysectomy in the dog, for example, gives rise to a strikingly selective atrophy of the procreative cells of the testis without much obvious structural loss of the sustentacular or interstitial cells. How much of the slowly evolved

clinical picture of physical inertia, heavy deposits of body fat, etc., is referable to the hypophysis and how much to the testicular atrophy is hard to determine. In the nervous system this distance effect or influence of a lesion in one part of the system on the function of other parts is of great importance. There can be no question that the various neurons of a given system—e. g., the kinesthetic group—are much more closely related physiologically than are two belonging to different systems and that there are therefore certain pathways of physiologic predilection over which nerve impulses tend to travel from selected end stations without great spread. This is one of the fundamentals of coordination. On the other hand, the action of strychnine and tetanus toxin, resulting in a condition in which stimuli applied to any receptor may lead to generalized convulsions, shows clearly the tremendously wide interconnection between systems. The effects of a lesion are naturally much more obvious in the related links of one physiologic chain, but in certain brain functions data from many fields are used to common purpose, and defect in any may influence others to a considerable degree. This is in evidence in the intricate problems of alexia, aphasia and agnosia.

The expression of this indirect effect on otherwise normal centers may, as in the direct, be either that of discharge or of defect, but more commonly it serves to modify the responses of other centers (diaschisis of von Monakow) or to uncover simpler mechanisms which have been hidden because of their subordination, under normal conditions, to those of a higher order. This reappearance of submerged reaction patterns I have called resurgence.

The following skeleton outline illustrated by a few examples will serve to indicate the nature of this problem:

I. *Direct or Local Effect.*—(*a*) Local Discharge: This is seen in certain cases of jacksonian epilepsy in which an irritative lesion over a restricted part of the motor cortex consistently gives rise to initial convulsive movements in the group of striped muscles which receive their voluntary innervation from that cortical area. Here, it is true, the effect is indirect as far as the spinomuscular neuron is concerned, but from the standpoint of the cortical level it may be looked on as a direct result of the irritation of the motor center.

(*b*) Local Defect: The total paralysis which occurs in disease of the anterior horn cells, the selective paralysis of voluntary movement which follows pyramidal tract lesions and the sensory deprivations which are caused by infracortical destruction of sensory pathways are all good examples of functional defects which are the direct results of local structural damage.

II. *Indirect Effect.*—(*a*) Indirect Discharge: In epilepsy associated with lesions of the cornu ammonis and other sensory areas we,

see evidence of the translation of discharge effect through structurally normal tissues. We envisage the convulsion here as the result of a normal response of the motor mechanism to abnormal discharges coming through from behind, so to speak, from damaged sensory areas.

(*b*) Indirect Defect: In tabes the coordinative control of the legs by the cerebellum is wanting, not because of disease of the cerebellum itself but because the defect in the gangliospinal neurons prevents the kinesthetic data from reaching that organ. That the cerebellum is competent for its task is indicated by the striking degree of compensation shown in many tabetic persons when using a cane. The cane and the arm furnish the cerebellum with sufficient data of position so that control of the sequential movements of the legs is greatly enhanced. Canes in either hand, moved forward alternately to obviate loss of contact during advancement, are naturally much more efficient.

(*c*) Abnormal Responses: The exaggeration of the knee reflex in pyramidal tract lesions is a quantitative example of abnormal response in the effector determined by defect in one of the paths which impinge on it. As another interesting probable example of this phenomenon I may suggest the tremor associated with disease of the basal ganglia. Here the lesions are predominantly degenerative, and especially in Wilson's disease and pseudosclerosis there is little of the fibrous gliosis which we have come to associate with the irritative type of lesion, and yet the tremor exists as a frank modification of normal movement suggesting a discharging or irritative reaction. The anterior horn cell is capable of responding over a wide range of rhythms, from discharges that result in slow writhing movements, such as athetosis, through all the range of voluntary movement to tetanic contractions, and even above this point the muscle note evinces a harmony between rate of response and rate of application of the stimulus. The pyramidal tract, however, is known to have a fixed rhythm of discharge of about 8 to 10 per second, which is well within the responsive range of the spinomuscular. Some mechanism must be inserted to prevent the rhythmic discharge of the pyramidal tract from impressing its rate during rest on all voluntary muscles. The occurrence of tremor through destruction of a part of the adjuvant motor apparatus (lenticular nuclei) suggests that this structure may normally act to smooth out movements of striped muscles. Still another possibility of entrancing theoretical interest comes forward in the consideration of hallucinosis. The normal mind is readily able to distinguish between sensory experiences in a given field such as vision, and mnemonic images from the same field. Sensory clarity probably rests on a simultaneous or immediately successive stimulation of the arrival platform (calcarine) cortex and the visual recognitive (visuopsychic) area. Overdetermination of the imagery, which would

readily account for hallucinosis, might occur from discharge by irritation of either the visuopsychic or the calcarine area, or might result from a disproportionate strength of the visual recognitive stimuli because of reduction in the visuosensory. The genesis of delusions is also frequently explainable on the basis of defect. Thus the delusions of senile dementia and Korsakoff's psychosis are often intimately related to the defect in memory implantation.

(*d*) Resurgence by Defect: This forms a particularly interesting group. In early infancy evacuation of the bowels and bladder is a purely reflex act which through training is brought under control of volition. The earlier reflex mechanisms, however, are in no wise altered by this training and are still competent to function when the dominant control from above is withdrawn as a result of extensive bilateral cortex lesions or of complete transverse myelitis. Betlheim has called attention to a similar uncovering of an earlier reflex pattern by defect in higher centers in the occurrence of a sucking reflex in patients with marked apraxia of the mouth musculature. In the early development of speech and voluntary muscular movement in the child, mimicry of the speech and gestures of their elders plays an important rôle, in fact, this is regarded as a separate stage of development. Echolalia and echopraxia, therefore, instead of standing out as distinctly bizarre parakinetic phenomena may in reality be only resurgent reactions due to a reduction of volitional control. That this volitional reduction is potent in catatonia, in which echolalia and echopraxia are most frequently encountered, seems obvious from other elements of the syndrome. Dorsal flexion of the great toe is a normal response to plantar irritation in the new-born child, and Kleitman has recorded it in normal young men in the very deep sleep that followed deliberate sleep-deprivation for a period of from 40 to 110 hours, and it therefore seems not improbable that the Babinski sign is also of a resurgent nature.

These examples emphasize the way in which the nervous system is built up as a pyramid of mechanisms, each autonomous in its own field, but each with its behavior under the guidance of those above. This warrants a cursory review of the general phylogeny of nervous structures.

PHYLOGENY OF NERVOUS STRUCTURES

Nature in her experiments in compounding single cells into more complex cooperative colonies seems to have been satisfied with her earlier achievements. She has not redesigned the whole nervous system in the mammals, for example, but has incorporated there mechanisms to serve lower functions which form the entire nervous equipment of organisms lower in the developmental scale, and for the further elaborated functions she has simply added higher centers, giving them directive control over the lower but not charging them with the duties of the simpler type.

The mechanism which she perfected in the jelly fish, for example, is repeated in the *Crustacea,* but here under control of a more complex system; both of these are repeated throughout the animal scale, and probably each cardinal evolutionary step in nervous development is recorded as a more or less independent system in the human equipment. It may be of value here to compare briefly these various phylogenetic steps with the similar structures in the more highly complex.

I. *Stage of Direct Muscular Responses.*—In the earliest stage of development of muscle cells known to us, that of the sponge, no nerve mechanism has yet been demonstrated. Apparently the muscle cells themselves are competent to respond to environmental changes without the intervention of nerve structures. No parallel to this stage is known in the adult forms of the higher animals, although the heart muscle probably passes through such a state in the embryo.

II. *Asynaptic Level.*—The swimming bell of the jelly fish, *Medusa,* contains muscle fibers activated by a nerve net. This is a true network of nerve cell filaments which are apparently continuous from cell to cell and not interrupted as in all higher nervous structures. Because of the lack of interruptions, this system is known as the asynaptic. Musculature innervated by such a net is characterized by a spread of a wave of response equally in all directions, and because of this diffuse spread the nerve net is said to have no polarity. In *Medusa* this net serves for the control of all reactions requiring speed of adjustment. An entirely homologous equipment is found in the intestines, blood vessels and probably in part at least of the intrinsic nerve tissue of the heart of higher animals.

III. *Ganglionated Cord Level.—Crustacea* are equipped with an intestinal and vascular control of the asynaptic type, but in addition they have a pair of nerve trunks, dorsally placed, one on either side of the midline, which are beaded with collections of nerve cells. This ganglionated cord in these animals is charged with all of the higher functions of locomotion, etc., while the simple, so-called vegetative, functions are under command of the asynaptic. There is, however, coordination between these two systems, by connecting fibers from the higher which serve to bring the simpler reactions under guidance. The ganglionated cord of the sympathetic nervous system in the higher animal is homologous to this dominant structure of the crayfish.

IV. *Spinal Cord Level.*—In *Amphioxus* we find the beginnings of a brain, but the responses of this animal are largely governed by a central linear cord of nerve tissue arranged around a central canal and representing the spinal cord of the higher animals. Within this cord are the sensory cells, paths of longitudinal communication and motor nuclei. I am not aware of a description of the linkage between this cord and the

lower levels in *Amphioxus,* but in the higher vertebrates we find fibers running from the sympathetics to the posterior roots to enter the cord and arborize around cells within the cord which are set aside as separate nuclei in the lateral horns. From here axons travel back as the white rami to the sympathetic ganglia. These two communicating links form the path over which the higher centers receive information from the sympathetic system and exercise control over its reactions. The fibers which arise in the lateral horn nuclei in the spinal cord (the preganglionic fibers) are the only ones of the sympathetic system which are equipped with medullary sheaths, and hence are easy to trace. Many of them end in the first ganglion which they encounter and arborize around sympathetic ganglion cells there. Others, however, pass through, and a few apparently pass well down with the nonmedullated sympathetic fibers toward their insertion. I think that the balance of opinion here, however, favors the view that all such preganglionic fibers are interrupted before they come in direct relation either with the asynaptic system or with smooth muscle, and operate through the intervention of cells of the sympathetic type. The relative autonomy of the spinal cord even in so highly organized a vertebrate as the dog is shown to excellent advantage by Sherrington's work with the reflexes in the spinal dog. Such accurate compounding of muscular responses as the extensor thrust and the scratch reflex can here be elicited from spinal centers in an animal with a high cord transection which cuts off all possibility of control from above. Sherrington has emphasized that it is probably by the compounding and orderly sequence of such motion patterns, resident in the cord, that voluntary movement is synthesized by the precentral cortex. He points out that the presence of a much smaller number of fibers in the pyramidal tracts than in the motor nerves supports this view.

V. *Midbrain Level.*—Most fish—the ganoids and teleosts—have practically no forebrain, and the function of vision, for example, which in higher forms is carried out by the occipital cortex, is here resident in the corpus opticum. From this level motor control paths travel back in these animals to the spinal cord leaving the latter with its full duty of commanding certain reflex patterns from which may be constructed the more complex movements, but taking from it the dominance or lead control. It is interesting to note that this phylogenetic step represented in its purest form today by certain fish (trout, for example) is marked in man by the insertion of a relay station between the visual tracts and the spinal cord. From the anterior pair of the corpora quadrigemina—from cells innervated by branches of the optic nerves—a group of fibers arises which travels through the posterior longitudinal bundle, the course of which has been traced to the anterior horn cells

of the cord from the nuclei of the third cranial nerves to the sacral region. This purely reflex path has obviously great possibilities in aiding to control motor responses in harmony with visual stimuli, and yet it must be looked on as a path with subservient relation to the dominant motor paths from the cortex. As we travel higher in the animal series

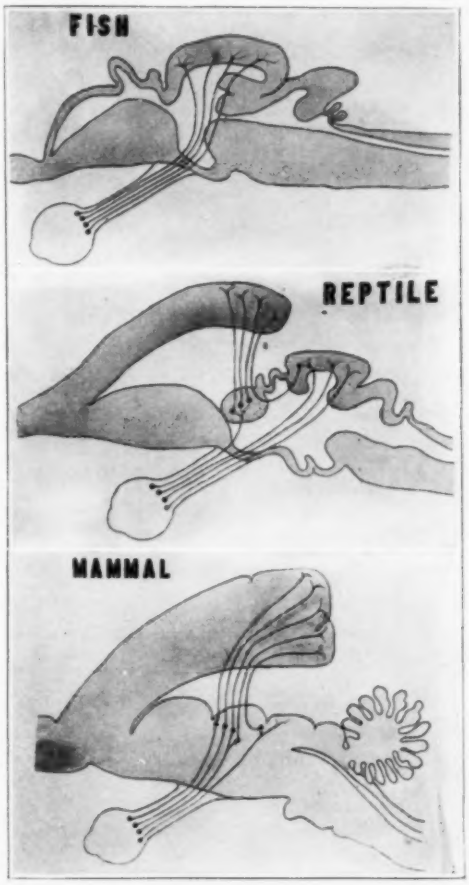

Fig. 2.—Scheme of optic connections in the brains of the fish, reptile and mammal. In the fish all fibers end in the corpus opticum; in the reptile a few are interrupted in the optic thalamus and relayed to the cortex. In the mammal the corpus opticum is represented by the anterior pair of the corpora quadrigemina and most of the optic fibers pass to the thalamus and by relay to the occipital cortex. (Modified from von Monakow.)

we find that a new relay station is developed at about this level; the optic thalamus. Figure 2, taken from von Monakow with some modifications, shows schematically the relationship of the corpus opticum, the optic thalamus and the occipital cortex in the trout, a reptile and a mammal. It is interesting to note that the thalamus which is present as low in the

series as certain fish is represented throughout the rest of the scale as a relay station in which all sensory paths except the olfactory are interrupted on their way to the cortex.

The motor component at this level is far from clear. In the lower fish and when the pallium has as yet not appeared the striking mass of

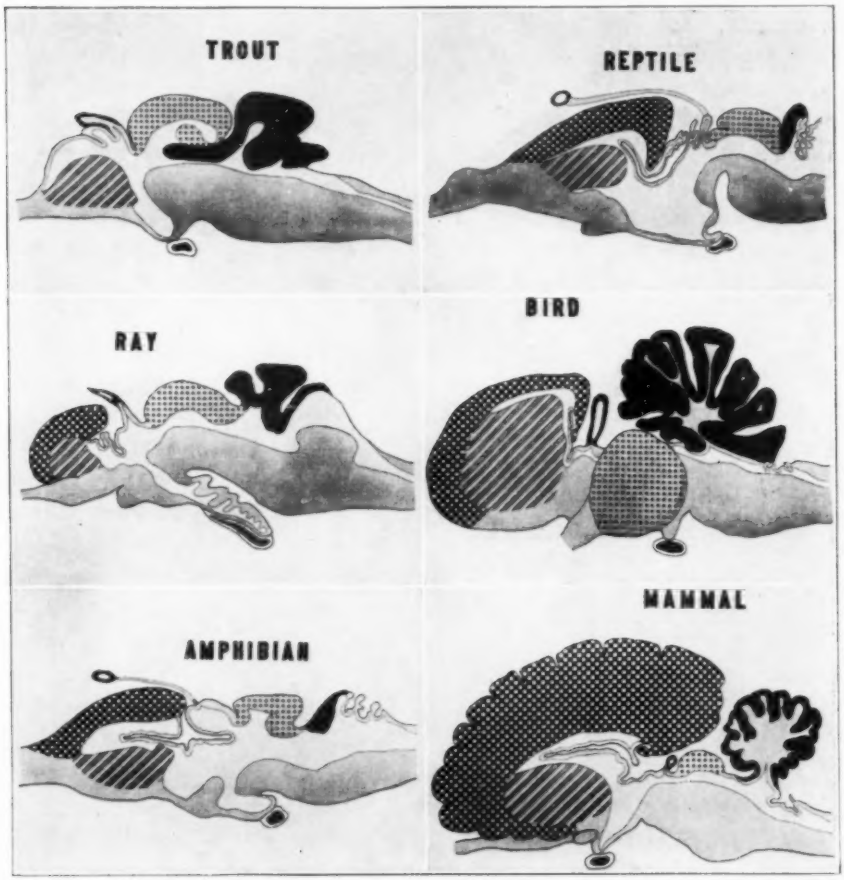

Fig. 3.—Schematic drawings of the brains of the trout; the ray; a reptile; a bird; an amphibian and mammal to show the relative development of various brain parts. The cerebellum is indicated by solid black area; corpus opticum, dotted; corpus striatum, diagonal stripes; pallium, checkered. (Modified from Edinger.)

the corpus striatum suggests itself as the midbrain motor organ, and its comparative prominence through the amphibians, birds and reptiles, in which cortical development is not advanced, also leads to this inference. In the mammals, however, in which control of motion has been lifted to the cortex, the great motor path from the cortex to the cord passes

this region without interruption, leaving the relationships less clear than on the sensory side.

VI. *Cortical Level.*—The fish show practically no pallium or cortical mantle, but, beginning with *Cyclostomata,* there is present a forebrain of increasing size and complexity as higher orders are reached. Figure 3, modified from Edinger, shows the relative developmental progress in a schematic way from fish to mammals. The relations of the corpus opticum, as shown above in von Monakow's diagram, can be followed through this series, as can the corpus striatum, the cerebellum, the choroid plexuses and other structures.

The earliest phylogenetic cortex is olfactory, but vision is also lifted into the mantle by the time the reptiles are reached. Commonly, the phylogenetic parallels are dropped with arrival in the cerebral cortex. I think, however, that we may tentatively at least hypothecate three fairly distinct levels in the mantle of man which probably correspond roughly with three levels of the mammalia. The reasons for this further subdivision will come out more clearly in our discussion of cerebral localization, but as a skeleton plan we may outline here these levels as: (1) The arrival platform, which is that area of cortex in which a sensory path first debouches and which is devoted selectively to sensation of one particular type. Apparently, however, this cortex subserves sensations only and is not associated with recognition of the meaning of sensory impressions. (2) The elaborative, or as I prefer to call it the recognitive, which extends as a zone around each arrival platform, and which apparently again is selective for one type of sensation and which probably serves in conjunction with the arrival platform for the recognition of concrete objects. (3) The associative areas, in which sensory material of various types is brought together to form the concept. It is probably here that the abstract memories are stored which serve as the building material for ideation, imagination and, when operating in harmony with the two lower centers, for the recognition of the meaning of graphic, verbal and other symbols.

Editorial

ASSOCIATION FOR RESEARCH IN NERVOUS AND MENTAL DISEASE

The Association for Research in Nervous and Mental Disease originated in 1920 in a group of neurologists and psychiatrists who long had thought that the usual type of neurologic society is discursive in its efforts, wasteful of time and energy and not sufficiently intensive in interest. Consequently, the founders of this association conceived and organized a new type of medical gathering which was at once a brilliant success. The meetings have been marked by keen interest, a most unusual amount of first rate scientific work and constant good fellowship.

Each meeting (two days) is devoted to a single subject. This subject is chosen by the commission from one to three years in advance. The various divisions and subdivisions of the subject are at once assigned to men especially well qualified to discuss them and to contribute the results of further original research. Each contributor is requested to forward to the program committee at least six weeks before the date of the meeting an abstract of his contribution; this is mimeographed and copies are distributed to members of the commission.

Following presentation of his communication, the author is questioned *ad libitum* by members of the commission. There is no open discussion. This plan has been found to save an enormous amount of time and avoid much *tedium vitae*. After the commissioners have finished, other members may present questions in writing through the commission. All questions and answers are recorded.

Following each meeting records of the entire proceedings pass to the editorial committee, which embodies everything of value, together with full bibliography, in the annual volume.

The following volumes have appeared: "Epidemic Encephalitis" (1920), "Multiple Sclerosis" (1921), "Heredity in Mental and Nervous Diseases" (1923), "The Cerebrospinal Fluid" (1924). The 1922 volume, "The Convulsive State," has not yet appeared. It is to be considerably amplified. The 1925 volume, "Schizophrenia (Dementia Praecox)," is in preparation. The subject for 1926 (December) is "The Cerebellum," in its various aspects. These volumes are, in effect, the last word on the subject and they have gradually increased in fulness. Volume 1 contained 258 pages, the volume on the cerebrospinal fluid over 600 pages.[1]

1. The Cerebrospinal Fluid, New York, Paul B. Hoeber.

Each year a compiling secretary, appointed by the president, collects all important new material concerning the subject assigned to him. This is presented to the association and then filed. In due time this material is issued as appendixes to the annual volume.

The program is by no means limited to the membership. Distinguished scientists in allied fields are invited to contribute and to sit with the commission. Nor is the membership restricted to practicing physicians. But the members' major interest is expected to relate to neurology or psychiatry.

The chief aim of the association is to foster and direct intelligent and coordinated research along one major line each year. To this end steps have been taken to establish a fund which it is hoped may become large enough to endow this continuous research.

The present officers are: Frederick Tilney, president; Foster Kennedy, vice president; Henry Alsop Riley, secretary-treasurer, and Thomas K. Davis, assistant secretary, all of New York.

Members of the commission are: Frederick Tilney, New York; Lewellys F. Barker, Baltimore; L. Pierce Clark, New York; Charles L. Dana, New York; Francis X. Dercum, Philadelphia; J. Ramsay Hunt, New York; Smith Ely Jelliffe, New York; Foster Kennedy, New York; Adolf Meyer, Baltimore; Stewart Paton, Princeton, N. J.; Hugh T. Patrick, Chicago; Lewis J. Pollock, Chicago; Bernard Sachs, New York; Sidney I. Schwab, St. Louis; William G. Spiller, Philadelphia; M. Allen Starr, New York; Israel Strauss, New York; E. W. Taylor, Boston; Walter Timme, New York; T. H. Weisenburg, Philadelphia.

Information may be obtained from the secretary, Dr. Henry Alsop Riley, 870 Madison Avenue, New York.

News and Comment

FIFTY-SECOND ANNUAL MEETING OF THE AMERICAN NEUROLOGICAL ASSOCIATION

The next meeting of the American Neurological Association will be held in Atlantic City, June 1, 2 and 3, 1926, in the Hotel Ambassador.

THE NATIONAL ASSOCIATION FOR THE STUDY OF EPILEPSY

The next meeting of the National Association for the Study of Epilepsy will be held in New York in the Hotel Waldorf Astoria, June 7, 1926.

THE AMERICAN PSYCHIATRIC ASSOCIATION

The American Psychiatric Association will hold its next annual meeting in New York in the Hotel Waldorf Astoria, June 8 to 11, 1926, inclusive.

AMERICAN ASSOCIATION FOR THE STUDY OF THE FEEBLEMINDED

The fiftieth annual session of the American Association for the Study of the Feebleminded will be held in Toronto, Canada, at the King Edward Hotel, June 3, 4 and 5, 1926.

THE AMERICAN PSYCHOPATHOLOGICAL ASSOCIATION

The next meeting of the American Psychopathological Association will be held in New York June 11, 1926, in joint session with the American Psychiatric Association.

Abstracts from Current Literature

MANIC-DEPRESSIVE INSANITY. JOHANNES LANGE, Klin. Wchnschr. 4:1577-1579 (Aug.) 1925.

As is well known, Kraepelin, in 1896, grouped together under the heading of periodic insanity the various periodic, circular and manic psychoses. Next came his grouping of manic-depressive psychoses. Since Kraeplin's classification, many minor and also radical changes have been suggested, but seemingly, as is only too apparent in the present writer's discussion, little change of value has evolved. It is, however, interesting to see how a subject may be mangled in the course of scientific investigation. The entire clinical picture of the manic-depressive psychoses suggests something uniform. Close observation reveals that melancholia with its manifold thought and volition disturbances and objective symptoms, and mania with its brilliant moods, flight of ideas, etc., not only merge into one another, but also in mild and severe grades are to be seen in the same patient.

Most patients affected with a manic-depressive psychosis go through various phases; however, several years may elapse between attacks and it is not uncommon for some persons to be visited with only one attack of melancholia or mania in a lifetime. The mild cases, of course, are recognizable only to the specialist. These may last days or even years. They all get better, or at least do not of themselves lead to marked reactions. When one considers that the various clinical forms observed are not dependent on outside influence but are of an hereditary character, the thought must occur that a potent disease process is at work.

Lange takes up the various discussions which at present appear to him to merit consideration: 1. If one considered manic-depressive reactions only as a symptom-complex, then one might add to the manic-depressive group numerous conditions which show a manic or depressive trend. 2. Because of similar symptomatology, melancholia, paranoid conditions and compulsive states have been grouped under the manic-depressive heading by some writers. 3. It cannot be disputed that catatonic manifestations, in the broad sense, occasionally occur with manic-depressive psychoses and are outstanding in the disease picture. On the other hand, it is apparent that schizophrenic diseases might go on for years masked as manic-depressive psychoses. 4. Finally, of the psychopathies, such abnormalities as depression, hilarity, irritability, etc., have been pointed out as sufficient to place them in the manic-depressive group.

Since Kraepelin already expressed the opinion that it is simpler to consider the disease group as growing out of one general root with ready convergence into the various forms, it is no wonder that Kleist, as a pupil of Wernicke, is opposed to the symptomatologic power that lies in the attempt to unite all possible forms of periodic disturbances with the manic-depressive psychoses. He does not deny the relationship of these disturbances and calls them, according to Schroeder, indigenous degenerative psychoses, yet he himself wishes to separate the manic from the depressive form. The frequent combination of these forms he explains by saying that the questionable genotypes are inclined to attach themselves to the complex genotypes. The finer symptom investigation necessary in Kleist's theory promises to bear fruit, especially from the standpoint of localization.

Bumke has endeavored to include melancholia with the manic-depressive psychoses. He says that melancholia is not a purely endogenous disease. Of no little importance is his rejection of the contribution of G. Specht who saw in paranoia a form of manic-depressive psychosis. Bumke emphasizes that a sharp line cannot be drawn in functional psychoses. One must, therefore, be satisfied to group together functional psychoses of certain narrow types, as also manic-depressive psychoses. More fruitful, however, from a clinical standpoint are the theories of Specht. These tend to a dissolution of the complicated clinical forms and confusion states akin to the manic-depressive psychoses, which he is inclined to designate as manic-hysteric mixed pictures.

While the possibility of dementia praecox being in the same class with manic-depressive psychoses has been looked on unfavorably, Urstein has considered a large portion of manic-depressive psychoses as the forerunner of schizophrenia. Ritterhaus, thinking along the lines of Hoche, came to the conclusion that manic-depressive psychoses could not be looked on as a disease entity, but merely as a symptom-complex which various disturbances, even endocrine disturbances, may bring to the surface in similar forms. Ewald disputed this, although it cannot be doubted that manic-depressive manifestations may be symptom-complexes of more or less specific significance. However, in the face of all the pros and cons of the question, all authorities agree that the actual cause of disease or the harmonious blending of similar causes is not the only determining factor, but that any number of things must be considered in making up the entire picture—the personality, history, environment, etc. Bierhaum has investigated the question in its minutest detail, but sufficient clinical work has not yet been done to warrant definite conclusions.

Thorough clinical investigations of Reiss, in 1910, have demonstrated the close relationship of morbid personalities and the formation of psychoses, in that their starting point is a constitutional discord. Kretschmer's work is more far reaching since, in viewing the mental personality, he takes into consideration the bodily structure and its relation to the psychoses, and this forms the center of his investigations. The history of heredity has enabled him to see in the severest cases of manic-depressive psychoses a great connection with certain normal temperaments.

In the study of bodily structure, with a vast amount of material Kretschmer proved that manic-depressive persons have a certain definite form, characterized by wide body cavities, inclination to full rump with relatively trim extremities, soft wide facial type, good plastic, healthy skin and heavy hair — mirror-like baldness is frequent. On the other hand, he has found that the vast majority of these people possess a constant personality sign in a definite temperament. This "cycloid" temperament consists of frankness, easy inflection of the voice, which is either gay or sad — at times the one and then the other. These persons are usually big hearted, friendly and good natured, and when circumstances arise which are out of the ordinary they become either extremely gay, humorous and lively, or unduly quiet and serious. Kretschmer's investigations are corroborated by the genealogic works of Hoffman which are by no means complete. Hoffman found numerous cycloid types among the progeny of manic-depressive persons. The turn which Kretschmer has given the problem seems to have the greatest possibilities. Bumke once said if one thins out manic-depressive psychoses too much, "man" and "manic-depressive" would be synonymous. Kretschmer's investigations have met with hearty approval, but also with great disapproval. However, as long as the waves roll so high, a conclusive opinion is impossible.

Ewald takes up the biologic foundation of temperament and manic-depressive psychoses and wonders if it might be ascribed to the endocrine apparatus. Associated symptoms, puberty, climacteric, menstruation, etc., seem to be allied.

The evolution of manic-depressive insanity since Kraepelin has greatly extended, but Kraepelin had the right idea, and his creation remains intact and, by the impetus of its development, will occupy a greater realm.

MOERSCH, Rochester, Minn.

SUBARACHNOID HEMORRHAGES. J. ROTHFELD, Ztschr. f. d. ges. Neurol. u. Psychiat. **97**:443 (July) 1925.

The symptomatology of subarachnoid hemorrhages is very uncertain, chiefly because the condition is so uncommon. In addition to all the general and local manifestations of cerebral hemorrhage, the spinal fluid findings are of extreme interest in this disease as of diagnostic importance. The etiology of the disease is extremely uncertain, especially when it occurs in young and healthy persons. With these points in view, the author analyzed his material in order to obtain some definite knowledge.

Three cases are presented. The sudden onset of the disease with severe headache and loss of consciousness in a young, hitherto perfectly healthy person, with meningeal signs, at first without fever, is characteristic of a subarachnoid hemorrhage. Lumbar puncture confirms the diagnosis. Differential diagnosis includes epidemic meningitis, which is a strong possibility when outspoken meningitic signs and a temperature of 39 C. are present. Epidemic meningitis may come on suddenly, but the fever is high from the onset, and the course is progressively downhill and leads eventually to death. In one of the cases described there were apparently two hemorrhages, each followed by confusion, and the last one was followed by right hemiplegia with aphasia. The cause of the hemiplegia was compression of the left hemisphere by a hematoma followed by malacia. This seemed the more probable to the author because the hemiplegia developed gradually with disturbance in speech, then right facial asymmetry, and then paresis first of the upper and later of the lower extremity. The occurrence of hemiplegia in subarachnoid hemorrhages is not a matter of universal agreement. Fracassi did not see it once in eight cases, while Goldflam considers it a not uncommon complication. Flatau has observed a case with hemiplegia. Goldflam considers the prognosis of hemiplegia in such cases as favorable, an experience which is not corroborated by the author's case. The spinal fluid in this case differed from the other two — in the first examination it was very bloody and contained polymorphonuclear cells with no globulin. On the second examination it was very much less bloody, the globulin was positive, and the colloidal gold reaction was characteristic of nothing.

Rothfeld lays stress on the sudden onset of the illness. Goldflam has described it as a "brutal onset," in a previously healthy person without vascular disease, with apoplectiform attacks. The first symptoms are pain in the head and neck which is the outstanding complaint in the entire course of the disease. One patient complained of a feeling of an open wound in the skull and of pains in the vertebrae. The headaches were intolerably severe. With these symptoms occurred confusion which continued for varying periods. In one patient it lasted a few minutes, in another a few hours. In many cases no confusion occurred. In all three cases meningitic symptoms were present from the beginning: stiffness of the neck, positive Kernig sign and tenderness on compression over the eyes. Only in one case was fever present and

then only at night, and the temperature was never over 38 C. Fever is not a common symptom. The pulse is slow. Optic neuritis is rarely seen and was first described by Bittorf.

Localizing symptoms are usually present. One patient had a left hemiparesis with stereognostic disturbance in the left hand and paresthesias in the left upper extremity. Another had severe right hemiplegia with aphasia. Lesions in the internal organs were not present. The "massive albuminuria" of Guillain was not seen in the author's cases. Goldflam describes a case with no albumin shortly before the hemorrhage and with positive albumin in the urine after the hemorrhage occurred. Psychic disturbances are rarely seen in the course of the illness.

Lumbar puncture forms a very important part of the diagnostic procedures. The findings in this condition have been studied by Eskuchen, Goldflam, Meylan, Flatau, and Zand. The fluid is under high pressure. If the hemorrhage has ceased the fluid becomes progressively clearer and shows the slightest tendency to xanthochromia. In the beginning, however, it is definitely bloody. Centrifugalizing of this bloody fluid shows xanthochromia, a differentiating point from hemorrhage due to puncture. The fluid is clear after centrifugalizing only in those cases in which the puncture is done shortly after the onset. Moreover, while the fluid becomes progressively clearer in meningeal hemorrhage it is always bloody or xanthochromic. Fluid runs out more slowly in meningeal hemorrhage than in hemorrhage from injury of a vessel during puncture (Hennebey, Finkelstein). Flatau, Goldflam and Zand state that the Nonne-Appelt reaction is weakly positive or negative. They say, moreover, that the cells are at first polymorphonuclear and later become lymphocytes. The colloidal gold test shows nothing characteristic.

Differential diagnosis includes internal hemorrhagic pachymeningitis, serous meningitis or infectious meningitis.

The etiology of the condition is not clear. Arteriosclerosis seems to play no part in the condition. Löwy and Jaksch found a cerebral aneurysm in their cases. Meylan assumes a disturbance in the innervation of the cerebral vessels. Handelsmann and Rotstadt assume a congenital tendency to bleeding, etc. Goldflam could not find these symptoms, nor could the author. Goldflam found histories of migraine in his cases and remarked on the relation of the two conditions, migraine and subarachnoid hemorrhages.

ALPERS, Philadelphia.

VERTEBRAL CHANGES COINCIDENT WITH EXTRAMEDULLARY TUMORS. JOSEF ERDÉLYI, Klin. Wchnschr. **4**:1591-1593 (Aug.) 1925.

Extramedullary tumors do not involve the vertebrae and rarely cause changes visible with the roentgen ray. Pneumography, while of some help, does not always serve to localize the lesion. Therefore, indirect changes in the region of the tumor which are discernible by roentgen ray deserve attention. The ventrodorsal position is not sufficient in examination of the vertebral column, and in every case the author has completed his examination by a lateral oblique view. His contribution concerns only cases which came to operation because of well defined tumors of the spinal column. These changes may not be of great diagnostic value; however, they may give rise to a mistaken diagnosis.

It is recognized, mainly through the reports of Oppenheim, that tumors of the cord, the membranes, or the nerve roots may be accompanied by scoliosis and kyphoscoliosis. These changes have also been noted in gliosis and

syringomyelia. According to Assman the frequent occurrence of kyphoscoliosis in the last disease, which is usually at the neck or upper portion of the column, is undoubtedly referable to disturbed nervous influence and the simultaneous action of changed static strain. Textbooks on roentgen-ray diagnosis have had little to say regarding this neurologic problem, to which Erdélyi gives special attention.

In six cases of extramedullary tumor that came to operation, alterations of the vertebrae occurred at the level of the tumor in four, and at a somewhat lower level in two. In case 1 a firm bridgelike exostosis connected the body of the vertebrae. In cases 2 and 3 there was a spurlike exostosis, partly on the side and partly on the front angle of the vertebral body. In neither case was there any periosteal stratification, unevenness or hyperostosis. Three plates are reproduced to show the exostosis, etc. In six cases, new bone formation was encountered in the neighborhood of the extramedullary tumor. The changes described are, no doubt, such as are frequently seen in the column in connection with other diseases.

From the standpoint of differential diagnosis the vertebral diseases most frequently observed are those which cause the same clinical manifestations as an extramedullary tumor, and those in which the alterations are confined to a single vertebra or a small portion of the column. Therefore tuberculosis, syphilis and vertebral tumors are of first importance. In tuberculous diseases of the vertebrae there is sometimes an exostosis, but a primary destructive process is always present. Bone formation begins as a protection. For this reason, strong bridgelike or bowshaped bone spicules are most frequent. These spicules prevent the sinking in of the diseased vertebra and cause rigidity, which is necessary for the healing of the process. Numerous cases examined by roentgen ray prove that isolated exostoses, osteophytes or diffuse hyperostoses do not occur in vertebrae that are otherwise roentgenologically healthy.

Spondylitis syphilitica also leads to the formation of exostoses. Oppenheim has reported a case of myelitis cervicalis accompanied by exostosis. This is a rare disease occurring chiefly in the neck vertebrae, but as a rule it does not cause such marked destruction of the vertebral body as does tuberculosis or tumor. The thornlike and similar exostoses accompanying extramedullary tumors resemble the changes frequently noted in older persons suffering from chronic arthritis.

It is the writer's opinion that these vertebral changes in extramedullary tumors are primary and not the result of any intercurrent affection. Between the wall of the vertebral canal and the dura mater there is an epidural mesh-work containing a complicated venous plexus. In this mesh-work are connections between the veins of the cord and the vertebral bodies. In the presence of an extramedullary growth, vascular changes occur in both the cord and the vertebral wall. It is the author's opinion that the calcification and arthritic changes are secondary processes resulting from venous stasis and hemorrhages produced by changes in the venous plexus.

Age plays no rôle in the development of exostoses as it has been noted in patients as young as 20 and 24 years.

As a rule the exostosis occurs at the level of the tumor, but in a small percentage of cases it has occurred a few segments lower. The conclusions reached are: (1) extramedullary tumors cause numerous changes of the vertebrae in the form of circumscribed or diffuse bone formation; (2) the formation of exostoses extends only to certain vertebrae and as a rule is in the region of the tumor; (3) the exostosis is caused by chronic inflammation and venous stasis of long standing in the region of the tumor.

MOERSCH, Rochester, Minn.

ANATOMIC CHANGES IN HUMAN RABIES AND THEIR RELATION TO THOSE OF EPIDEMIC ENCEPHALITIS. I. SCHÜKRI and H. SPATZ, Ztschr. f. d. ges. Neurol. u. Psychiat. **97**:627 (Aug.) 1925.

Schaffer describes three stages in the pathologic anatomy of rabies: inflammatory changes in the first stage; then degenerative changes in the nerve cells, and finally changes in the cells, producing the characteristic negri bodies. Porsche and Benedek believe that the negri bodies represent merely a product of the degenerated nerve cell. The authors, therefore, divide the pathologic findings in rabies into inflammatory and degenerative changes. Of the former, Meynert, Forel and Gowers mention perivascular infiltration as characteristic. The infiltrating cells are lymphocytes, a few plasma cells and fewer polymorphonuclear cells. Accompanying the infiltration is an overgrowth of glia, in part diffuse and in part focal, forming the so-called Babes nodules which are supposed to be characteristic of rabies. Schaffer claims that the degenerative changes need not be proportional to the inflammation. One often finds extensive inflammatory changes with a slight degree of degeneration in the nerve cells and vice versa. In fact, independent degenerations may occur. The microscopic picture shows lightly staining cytoplasm, pyknotic nuclei and changes in the nucleolus, together with vacuole formation, sclerosis, pigment atrophy and other changes.

Only a few contributions have been made to the pathologic study of human rabies. Achucarro reports a case in which the degenerative changes were very slight, but in which regressive glia changes were present, especially an increase in the microglia of Hortega. Klarfeld, in 1922, pointed out that the changes in epidemic encephalitis are of both inflammatory and degenerative nature, and that he had found changes similar to those of encephalitis in two cases of human rabies. In one case the inflammatory changes were limited to the pons and medulla while degenerative changes were found in the cerebrum and cerebellum. In the other case Babes nodules and slight infiltration were present in the spinal cord, while degenerative changes were present in the cerebrum and cerebellum. Achucarro has remarked on the similarity of findings in general paralysis and trypanosomiasis.

The authors report two cases The first was that of a man, aged 36, who was bitten by a wolf, the right eye being completely destroyed. Two weeks later definite signs of rabies developed, and two days after this the patient died. Necropsy revealed hyperemia of the meninges, slight dilatation of the ventricles and numerous punctate hemorrhages. The inflammatory changes were most intense in the substantia nigra. Almost all the vessels showed infiltration. The red nucleus showed few evidences of infiltration, and the same was true of the region of the oculomotor nucleus and the gray matter about the aqueduct. Nowhere was the inflammation as intense as in the substantia nigra. Caudally, it was present in the tectum of the pons and medulla, but only locally and by no means as intense as in the substantia nigra. The inflammatory cells consisted chiefly of lymphocytes with many polymorphonuclear cells, limited entirely to the adventitia, though many polymorphonuclears were free in the network of the substantia nigra. Babes nodules were found, in the center of which was a clear area probably representing the locus of a degenerated nerve cell, while around this was a wall of lymphocytes and glia cells. Degenerative changes were of a secondary nature. No negri bodies were found.

The second case was that of a child, aged 9, who was bitten in seven places by a jackal. Twelve days later rabies developed, and two days after this the patient died. Necropsy showed marked hyperemia, and a slight increase

in the fluid. As in the first case the inflammatory changes were limited chiefly to the midbrain and in particular the substantia nigra. Very marked degenerative changes were present in both the ganglion and the glia cells, in no way dependent on the inflammatory changes which they far exceeded, and almost universal in their distribution.

The authors call attention to the similarity of the findings in their two cases of rabies to those of epidemic encephalitis. In the first case the pathologic picture resembles encephalitis so closely that one could hardly tell the difference except for the aid of the history. The widespread degenerative changes in the second case are often found in encephalitis. The authors state that Babes nodules are not characteristic of human rabies.

ALPERS, Philadelphia.

OBSERVATIONS ON SPINAL AND DECEREBRATE KNEE JERKS, WITH SPECIAL REFERENCE TO THEIR INHIBITION BY SINGLE BREAK SHOCKS. L. BALLIF, J. F. FULTON and E. G. T. LIDDELL, Proc. Roy. Soc., November, 1925, pp. 589-607.

Simultaneous torsion wire myograph and electrical records were obtained of knee jerks in decerebrate and spinal cats and an analysis was made of their characteristics and of their inhibition by single break shocks. The mechanical response of the spinal jerk is two or three times longer than that of the decerebrate. The curve of relaxation of the spinal jerk forms a sharper angle with the plateau of contraction, yet has a less steep but smooth decline, while the decerebrate jerk relaxes with a speed approaching that of a motor twitch to about half relaxation when a hump appears which is interpreted as shortening reaction. The electrical response, though apparently single, tends to be more prolonged in the spinal knee jerk. The latency is greater in the spinal (8.8 thousandths of a second) than in the decerebrate (6.6 thousandths of a second). The spinal jerk is more difficult to elicit than the decerebrate. From the greater duration of the spinal knee jerk, the authors infer that it is produced by a repetitive discharge of at least from four to eight volleys of impulses recurring somewhat asynchronously at from 100 to 200 per second. The decerebrate jerk partakes more of the character of a motor twitch, though occasionally it too appears to be made up of two or even three volleys of impulses.

The spinal jerk is more readily inhibited than the decerebrate, the effect of a single break shock lasting from one to three seconds. The shortening reaction appended to the decerebrate jerk is readily inhibited. In two knee jerks of equal size (tension) but differing shape, the larger electrical response is observed in the jerk in which the point of inflection of the mechanical ascent is the lowest and in which the angle denoting onset of relaxation is the sharpest. This is interpreted as indicating that in the latter case, the first volley of impulses producing the response is the more synchronous of the two. According to this criterion a knee jerk recovering from inhibition appears to be more synchronously produced than an uninhibited knee jerk.

Of the many interesting results of this accurate analysis, the following may be selected for brief comment: (1) the response of the decerebrate is less synchronous than that of the spinal animal; (2) it is less readily inhibited; (3) it is briefer; (4) it is followed by a shortening reaction. The first two points may both be due to the presence of tonic extensor reflexes in the decerebrate animal. If the volley of afferent impulses finds a certain proportion of efferent neurons in absolute refractory phase, these will be unable to respond as promptly as others. The same factor would oppose inhibition on the principle of algebraic summation.

The longer duration of the plateau of tension in the spinal preparation is a somewhat surprising result. May it not be due to a double volley of afferent impulses? Such a possibility is suggested by the fact that a much stronger stimulus is required in the spinal than in the decerebrate cat. Even a single break shock, if strong enough, may set up more than one volley of afferent impulses and a strong mechanical stimulus may do the same. To do so it need not outlast the total irresponsive period provided it sets up a local excitatory process which does so.

Of even greater interest is the presence in the decerebrate cat of a shortening reaction under conditions admitting but a minimal degree of shortening. At first sight, such a combination seems strongly to favor the theory that the stimulus inducing the shortening reaction is change of tension. Yet it does not disprove the possibility that change in length, shortening and thickening of muscle fibers, rather than change in tension, affords the adequate stimulus. A torsion lever is never completely isometric. To the minimal shortening from movement of the lever must be added a further increment of shortening from stretch of the tendon by the high tension developed (about 2 Kg.). Such an interpretation is supported by the fact that the greater the amount of shortening allowed, the higher is the hump as a result of the shortening reaction (personal communication).

McCouch, Philadelphia.

Hepatolenticular Degeneration. A Clinical Anatomic and Experimental Study (Continued). Ivan Mahaim, Schweiz. Arch. f. Neurol. u. Psychiat. **17**:43-62, 1925.

Mahaim continues his discussion by reporting the case of a boy, aged 9, free from hereditary abnormalities, and a brother, aged 5, both in good health. About two years before, he was hospitalized because of mental deficiency and misbehavior. Up to this time his mental attainments were normal and he was at the head of his class. He had suffered a fracture of the thigh a few months before, after which he spoke less frequently, cried easily and exhibited a slight tremor. On examination, his handwriting was found to be tremulous, he did not speak spontaneously, his emotional reactions were fickle, the reflexes were active and on movement there was a generalized hypertonicity. He was discharged with a diagnosis of imbecility. One month before death he was readmitted, at which time he was emaciated and dysphagic, and exhibited a marked generalized hypertonicity and extremely slow and athetosic movements. The reflexes were difficult to elicit; the Babinski phenomenon was negative; no tremor was noted. He became steadily worse, developed a hyperpyrexia and died.

Necropsy disclosed a marked atrophic cirrhosis of the liver, many newly formed bile passages and proliferation of connective tissue with formation of nodules throughout. The hepatic cells did not appear to be altered. The cerebral lesions were limited almost entirely to the striate body. A bilateral lacunar condition involved the greater part of the globus pallidus; hemorrhagic lesions were noted in the putamen which appeared to be reduced in volume. The cerebral cortex showed some discrete alteration of the ganglion cells and a slight generalized proliferation of the glial elements. The hypertonicity with athetosis and spasmodic contortions were attributed to the pallidal involvement.

Jakob reported a detailed study of extrapyramidal motor disturbances. In Huntington's chorea the striatum and the cerebral cortex were found to be involved. Two cases of paralysis agitans complicated by unilateral athetosis

were reported by him. Necropsy disclosed diffuse lesions of the striatum and pallidum and a necrotic area in the pallidum opposite the athetosic side. According to him, athetosis only appears if the pallidum is markedly involved. In congenital double athetosis the situation is more complicated and the pathogenesis cannot be reduced to a single constant lesion. Recently Wimmer reported a case of pseudosclerosis without hepatic cirrhosis; however, this case does not withstand scrutiny for it resembled Friedreich's paramyoclonus, and it is difficult to form a satisfactory opinion of the exact pathologic changes found from his description. A similar criticism applies to cases of torsion spasm without hepatic cirrhosis reported by Richter, Cassirer and Westphal.

The parallelism of hepatolenticular degenerations remains a mystery. Wilson regards the hepatic degeneration as primary. The liver, he believes, produces a toxin which acts in a deleterious manner on certain portions of the brain. He is of the opinion that the affection is acquired in spite of the fact that it appears to be familial. Other writers lay more stress on the familial characteristics of this malady. Some believe that the liver and brain changes develop simultaneously as the result of a common noxious agent. One of the curious features of the hepatic cirrhosis is that it produces no clinical signs. Occasionally a slight icterus may be noted.

Mahaim undertook some experimental work to see whether he could produce hepatic cirrhosis by introducing a toxic substance into the biliary passages. He found on preliminary injection with methylene blue in a rabbit or dog that the biliary passages may be infiltrated to the finest ramifications. He next introduced 50 per cent ethyl alcohol through a biliary fistula formed by suturing the gallbladder to the abdominal wall. The liver of a dog so treated showed a marked generalized biliary pigmentation, necrosis and connective tissue reaction. (*To be continued.*)

WOLTMAN, Rochester, Minn.

SYSTEMATIZED DISTURBANCE OF ASSOCIATED MOVEMENTS OF THE EYES AND THE LIMBS OF PURE LABYRINTHINE ORIGIN. JEAN TARNEAUD, Rev. d'oto-neuro-ocul. **1**:183 (March) 1923.

A woman, aged 24, following a radical mastoid operation on the right side complained of headache and vertigo. There had been slight vertigo before the operation. Examination revealed a healed radical operative scar on the right side; total deafness in the right ear; left ear normal; no spontaneous nystagmus; in the Romberg test falling to the right. In walking with closed eyes, the patient deviated to the right. Convergence of the eyes was normal. In lateral binocular fixation of gaze the reaction was: to left, normal; to right, impossible. When she tried to followed an object moving from her left to her right at 20 cm. distance, the eyes were arrested in the median position. She was not able to fix with the right eye alone toward the right, but could do so with the left eye. With lids closed, if an attempt was made to move the eyes to the right, there was sudden vertigo. She was also unable to fix on an object situated to her right on account of a sensation of vertigo. If her head was turned passively to the left, the eyes did not attain a position of extreme lateral rotation to the right. If the head was passively turned and the patient was asked to look to the right, the eyes turned to the extreme right lateral position of the gaze (rotation of the head permitted movement of the motor oculi).

Vestibular Tests.—Rotation to the right caused intense vertigo lasting one-half hour, and the patient was unable to open her eyes. Rotation to the left caused nystagmus for five seconds; vertigo was marked but not so intense.

Water at 27 C. in the right ear caused violent vertigo immediately and the patient fell unconscious. In the fistula test compression and suction caused stupor; the eyes were tightly closed and prevented observation for nystagmus. When the region of the external semicircular canal was touched with a probe, vertigo but no nystagmus occurred. When a galvanic pole was applied on the right, with a current of 2 milliamperes, the patient fell to the right and backward, lost consciousness for fifty seconds, and had intense vertigo for three minutes; with the pole on the left with 2 milliamperes of current, she fell to the right and slightly backward and showed a fine rapid tremor.

Spontaneous Movements.—Movements of the right half of the body were difficult and were followed by a feeling of heaviness and fatigue in the articulations. Diadokokinesis was present and caused pain in the right arm. The arms when extended horizontally to the front with the eyes closed deviated slightly to the right, and this was not changed by altering the head position.

The eyegrounds were normal. Diplopia was present on looking downward only. The general examination gave negative results.

Four months later, vertigo was less; headache was persistent; pain and tenderness were present around the ear, and became exacerbated at the menstrual periods. The patient was unable to lie on her right side, could not bend, turn her head nor look to the right without dizziness and pallor; she deviated toward the right in walking. Movement of the limbs was painful, and accompanied by cramp in the biceps and flexor muscles of the right hand. When rotated to the right, she fell to the right; tinnitus and blockage of the eyes occurred. When rotated to the left, she fell forward, experienced tinnitus and showed pallor, nausea, rapid pulse and blockage of the eyes. When small doses of opiates were administered she improved. In a year she was well, without vertigo or ocular troubles.

The author concludes that: the clinical facts pointed to a peripheral labyrinthine lesion, which caused trouble with the ocular movements; a lesion of the external semicircular canal corresponds to a limitation of the lateral associated movements of the eyes and lack of coordination in the limbs; the clinical facts as well as physiologic and experimental data demonstrate that the semicircular canals command direction of coordinated motor acts; equilibration and orientation are proved to be functions of the semicircular canals.

DENNIS, Colorado Springs, Colo.

THE CONDITIONED REFLEXES AND CHILDREN'S NEUROSES. N. I. KRASNOGORSKI, Am. J. Dis. Child. **30**:753 (Dec.) 1925.

This contribution by a pupil of Pavlov details the application of some of the latter's work to the study of conditioned reflexes in children.

CASE 1.—In a child, aged 6 years, a conditioned reflex was formed after six trials. The motor phase of the reflex consisted of opening the mouth. It was established at the time of feeding and was associated with the sound of a metronome beating 144 times a minute. A metronome beat of 92 was unaccompanied by feeding during the trials and was therefore inactive. When now the child was allowed to hear at an interval of two minutes, first a metronome of 144 beats and then one of 92, it showed no signs of discomfort. When the differentiation became more difficult, i. e., between 144 and 122, the child became angry, fought with other children, and wanted to be discharged from the hospital. When the differentiation became still more difficult, i. e., between 144 and 132 beats, the child yawned and fell asleep. The case illustrates the development of: (*a*) widespread irritative phenomena in the presence of a

difficult task, the excitation spreading from the rather localized area of the cortex associated with opening the mouth to involve probably all the cortex; (*b*) complete inhibition when the task becomes still more difficult.

CASE 2.—A conditioned reflex was formed in a child, aged 6, by giving food five seconds after the metronome had started. The food was then delayed for successively longer intervals. When thirty seconds was allowed to elapse before the food was given, the reflex lost its stability and disappeared; intense general inhibition developed, the child yawned and went to sleep. When the experiment was repeated from the beginning, it was found that the reflex could be delayed sixty seconds before sleep developed.

CASE 3.—The child, aged 12, was suffering from hysteria. When it was attempted to set up a conditioned reflex as in previous cases, it was found that the mere stimulation of the metronome produced intense excitement, expressed by dyspnea, cyanosis and twitching of the facial muscles. A second attempt produced less excitement, a third still less; a fourth produced sleep, which lasted about two minutes after the stimulation had ceased. In this case, therefore, cortical functions were so unstable that not only was no conditioned reflex formed but also the simple type of stimulation by a metronome produced the extreme of intense excitement and intense inhibition.

CASE 4.—The patient, a boy, aged 6 years, was suffering from a conduct disorder following epidemic encephalitis; attacks of excitement occurred in which he broke window panes, tore his clothes and destroyed objects. These attacks occurred whenever he encountered any resistance. Conditioned reflexes in this child were found to be formed more quickly than in normal children; on the other hand, the processes of inhibition were deficient. In other words, there was a disturbance of balance, so that the child was more readily affected by excitatory stimuli and less readily affected by inhibitory stimuli.

The author points out the desirability of training the child from its earliest years to form inhibitory reflexes and to limit irritation, because "all discipline and education is an uninterrupted limitation of reaction by inhibition." The physician is advised to consider the individual inhibitory power of the child as opposed to the reflex that is selected for inhibition, as a lack of appreciation of the relative values of these factors forms the basis of frequent neuroses. The physician must know the conflict before he can cure the neurosis; in the experimental cases the conflict was removed by rest and was followed by restoration of balance.

VONDERAHE, Cincinnati.

ELECTROCUTION. ARGYLL CAMPBELL and LEONARD HILL, J. Indust. Hyg. **6**:267 (Nov.) 1924.

Counter shock as a method of resuscitation after electrocution has attracted considerable attention of late, many authors having pointed out that if the victim has fallen from a height he is more likely to recover. There being no obvious scientific reason for this, the medical profession has passed it over, and Drinker has said that if there is any difference in effect it is probably because the man on the pole "drops away from the source of current" more quickly than the man on the ground. In addition, the heart may escape a fatal shock, the charge coming through one rather than through both legs.

The authors describe a method of counter shock which has been accorded considerable publicity in Great Britain and is called McLaglan's system. It was described briefly by John A. Brown, a layman, as follows: With the thumbs placed at the pectoral arch and the subject supported by the operator's

knee, pressure is applied with both thumb and fingers upward and downward. This is continued for some time to stimulate the cardiac nerves, causing the diaphragm to expand and contract slightly, and making the patient inhale and exhale. As the thumbs are applying pressure in their up and down motion, the operator's knee delivers a blow on or about the seventh dorsal vertebra to further stimulate the action of the diaphragm and thereby to dilate the heart to its fullest capacity and circulate the blood through the body. A further stimulus is added by a shouting out as the blow is delivered, the auditory nerves being involved this time.

Although, as the authors say, there are obvious unsupported claims and anatomic inaccuracies in this description, the fact that it has gained such wide publicity and has even been given favorable reception by engineers led them to test both this method and the effects of a fall from a height. The authors applied electrodes to the head and left hind paw of a cat, after which a shock, of thirty seconds' duration, was given from an alternating current of 50 cycles, 210 volts. If there were no signs of respiration or heart beat within sixty seconds, resuscitation was instituted, with the following results: of twenty-eight cats, eight recovered spontaneously; McLaglan's system failed in five others after thirty minutes' trial; five others failed to revive after being dropped from a height of from 8 to 9 feet to a stone floor. In the remaining ten cats, the usual physiologic method of artificial respiration (rhythmic squeezing of the chest wall and massage of the heart through the chest wall) was performed for thirty minutes, with two recoveries and eight deaths. Two animals gasped during the latter method but could not be revived.

The authors conclude that: "Natural (or accidental) resistance of the heart to fibrillation would appear to afford the commonest means of escape from death by electrocution; counter shock is of no value in resuscitation, and there is no evidence that the standard physiologic methods should be altered."

The concluding paragraph states that ventricular fibrillation is the cause of death in electrocution. The only method of resuscitation recommended to the layman is that of Schäfer: the rhythmic squeezing of the heart, as well as the lungs, restoring the natural heart beat. Suprarenal extract injected directly into the hearts of electrocuted animals, while successful in some cases, is impractical. Their final conclusion is that an electric shock sufficient to throw the heart into fibrillation will continue to cause death in most cases. A bibliography concludes the article.

CHAMBERS, Syracuse, N. Y.

INTRAVENOUS INOCULATION OF MALARIA. R. NYSSEN, J. de Neurol. et de Psychiat. **9**:569 (Sept.) 1925.

Malarial inoculation in the treatment of general paralysis is now widely practiced. Most authors have used the method of injection and scarification, and its very simplicity has made it preferable to all others, especially to von Jauregg and his school. The method employed with the first patients treated by von Jauregg was scarification, which is very uncertain; it was soon replaced by subcutaneous injection. Mühlens, and after him Weygandt and Kirschbaum, used a very complicated method. They withdrew 10 cc. of blood from the donor before a febrile attack, and to this added 0.1 cc. of a 50 per cent solution of dextrose. After this the blood was defibrinated, placed in small tubes and injected subcutaneously at intervals of from one and one-half to three hours. By this method the hematozoa remain alive for more than three hours. Kirschbaum has demonstrated that the hematozoa of Laveran will remain alive

for twenty-four hours if to each ten parts of defibrinated blood one part of a 50 per cent solution of dextrose is added, and the mixture kept at 37 C. Kirschbaum first used intravenous injection and then studied the period of incubation. He used citrated blood from malarial patients. Mühlens in 1923, in a resumé of his studies, reported successful inoculations in 90 per cent of his patients by the subcutaneous method, with an incubation period of from five to thirty days, most of the cases being from ten to fifteen days.

All authors who have used the malarial treatments have reported great variability in the period of incubation. Kirschbaum reports it as varying from six to thirty-one days, Mühlens five to thirty days, Weygandt and Kirschbaum ten to twelve days, Kirschbaum and Kaltenback eight to fourteen days and Nonne twelve to fourteen days, and Weygandt and Kirschbaum have even reported a period of incubation of nine and one-half weeks. The author found an average period of incubation of 11.4 days in twenty-five patients.

The reasons for these variations are as follows: 1. The degree of receptivity depends on the race. The black race and Arabs resist malarial infection much better than Europeans. 2. Debilitating factors favor receptivity. 3. Wagner von Jauregg believes that the incubation period increases with the number of passages of the parasite through the human body. 4. According to Graham-Smith, Kirschbaum and others, the duration of incubation is a function of the adaptation of the parasite to its host. 5. The number of parasites inoculated affects the incubation period.

In twenty-six patients treated intravenously by the author no accidents were encountered. The average period of incubation was 11.4 days; the longest period was fifteen days; fourteen lasted only six days.

ALPERS, Philadelphia.

INTRACRANIAL CALCIFICATION PROBABLY IN A TUMOR IN THE REGION OF THE PINEAL BODY. E. MEYERS, M. J. Australia **2**:275 (Sept. 13) 1924.

Meyers presents a case in which the patient had pain in the temples, after which he received a blow, and following this had pain in the head for three months. He had a masklike appearance (Gordon Holmes in Osler's Medicine, comments on a masklike appearance encountered in lesions involving the tegmentum). The patient was found to be nervous and seemed to be deaf, but on examination was not. The eyes gave negative findings. Babinski Weil-Wallsing tests showed a definite deviation to the left. There was no Romberg sign, past pointing or adiadokokinesis. The knee jerks were normal and there was no clonus. The plantar response on both sides was flexor. The patient had definite paresis in the muscles of the left arm, forearm and hand. There was some confusion of the thermal sense in all four extremities. A tentative diagnosis was made of brain abscess because of the onset following influenza, recurrent mild rigors and paresis. Several distinct features, however, seemed to rule out this diagnosis, and then it was thought that there was a small tumor in the region of the right cerebral hemisphere. The history did not favor this but the signs did. A decompression operation was done. An opening was made, the bone divided and the flap elevated, fractured at the base and turned back. The dura mater was opened and the cerebrospinal fluid was found to be not under excessive pressure. The hemispheres were normal. A hemorrhage followed, so further procedure was not indicated. The patient made a satisfactory recovery, the only disability being a foot drop on the left side. The headache and giddiness also disappeared. The roentgenograms showed a probable tumor of the pineal body.

Cases of intracranial calcification are rare. Miller (Calculi Within the Brain, Surg. Gynec. Obst. **34**:786 [June] 1922) reported one case of calcification with a successful operation and recovery; and up to 1916 only seven cases had been reported. Dandy (An Operation for Removal of the Pineal Tumors, Surg. Gynec Obst. **33**:113 [Aug.] 1921) wrote that the symptoms are those of intracranial pressure, due to an internal hydrocephalus, which is caused by the occlusion of the aqueduct of Sylvius. He recommended operative removal and found no benefit from decompression.

FAY, Philadelphia.

ACUTE SYPHILITIC RADICULITIS WITH THE SYNDROME OF FROIN. R. DEBELKE and L. VAN BOGAERT, J. de Neurol. et de Psychiat. **8**:525 (Aug.) 1925.

A man, aged 21, had had pains in the lumbar region for five days followed by pains in both legs. Examination showed the right leg in adduction and semiflexion, and the left leg slightly flexed. Violent pains radiated down the leg. The vertebrae from the first lumbar to the second sacral were tender. The Achilles, patellar and abdominal reflexes were absent. A zone of hyperesthesia extended from the area of distribution of the twelfth dorsal to the second lumbar roots; below this was hypesthesia involving the legs and feet. Lumbar puncture revealed a fluid under great pressure, slightly xanthochromic and containing many polymorphonuclear cells. The Wassermann reaction with the spinal fluid was positive on three occasions. During his stay in the hospital, in the course of from one to two days, the patient developed severe pain in the course of the sciatic, crural and abdominal cutaneous nerves, with a positive Laessec's sign on the right. The sensory disturbance cleared up almost completely, the cell count in the spinal fluid fell from 172 to 94, and the fluid became clear. The fever which had been present from the beginning persisted, as did the positive Wassermann reaction. The authors looked on the case as an acute lumbosacral radiculitis with Froin's syndrome. Despite the absence of lymphocytosis in the spinal fluid, the authors thought the process was probably syphilitic. Arsphenamine did not abort the course of the disease. There was some amelioration of the sensory and motor disturbances, but from observation of other cases the authors believed that the tendency was toward a spontaneous betterment. They incline to regard the condition as a syphilitic process rather than an acute process superimposed on the syphilitic disease, which was undoubtedly present.

ALPERS, Philadelphia.

SUGGESTION AND PERSONALITY. WILLIAM BROWN, Brit. J. M. Psychol. **5**:29 (May) 1925.

The Salpêtrière school (Charcot, Janet) puts mental dissociation as the cause of the increased suggestibility which is observed in hypnosis, whereas the Nancy school holds that hypnosis is due to artificially increased suggestibility, and offers no explanation of the phenomena. The authors feel that the experiences of the war support the explanation of the Salpêtrière school. This mental dissociation can be brought about not only by mental conflict and repression, but also by physical factors such as shock to the brain. Such a person can be hypnotized with exceptional ease, and there is no obvious psychologic reason for it.

If we accept Babinski's rather crude view that hysterical symptoms are due to suggestion and hence curable by persuasion, why the individual is so susceptible to the influence of autosuggestion is still unexplained. This explanation is to be found in the desires of the patient's mind, which rest on a

mental conflict. The hysterical symptoms resulting represent a compromise and a temporary solution of the difficulties.

Brown does not accept Freud's formulation that suggestion and suggestibility is a form of transference similar in nature to the relationship which existed between parent and child. This is in accordance with Freud's theory of group psychology, in which the leader holds his position because of the libidinal ties existing between him and the members of the group. Brown feels that the transference situation is one of the conditions under which suggestion can occur. Suggestion can occur, however, when there is no transference. He has strong doubts about suggestion always having a libidinal relationship.

ALLEN, Philadelphia.

INDUSTRIAL PSYCHIATRY. HENRY B. ELKIND, J. Indust. Hyg. **6**:251 (Oct.) 1924.

In this article Dr. Elkind has emphasized the following points: 1. Industrial physicians are coming to realize the importance of psychiatric work in their medical tasks. This work consists of a study of the personality and a history of the mental, physical and social factors, by which many cases of functional nervous disorder can be cured. 2. More exact diagnoses are required for successful prognosis and treatment; heretofore there has been a tendency to diagnose all cases of nervous and mental diseases as "nervous disease, functional" on the part of industrial physicians. 3. Minor deviations of personality are important in that, if treated in time, they often will not progress to more serious mental disease. 4. Industrial psychiatry must not be mistaken for mental hygiene in industry, the latter concerning itself with the mental and physical health of workers.

Three cases are presented to illustrate the possibilities of industrial psychiatry: (1) headache — reclaimed through psychotherapy, the patient having repeatedly observed her mother dodge unpleasant situations through the medium of a headache; (2) prolonged mourning over death of husband — psychotherapy was at first resisted, but later the patient cooperated when an interest was found for her; syphilis was suspected but not proved; (3) suspected heart disease — the patient worried about her son who had become a victim of alcoholic insanity; prevention was stressed in this case because of a strong psychopathic taint in the patient's family; she is making a good adjustment under psychotherapy.

CHAMBERS, Syracuse, N. Y.

EXPERIMENTAL TETANY AND DIET. T. INOUYE, Am. J. Physiol. **70**:524 (Nov.) 1924.

In a large series of thyroparathyroidectomized dogs, observations were made relative to the effect on the consequent tetany of certain carbohydrate food stuffs in varying combinations. The carbohydrates used were sucrose, glucose, dextrin, lactose and galactose, given in association with varying amounts of casein. Inouye found uniformly that with diets containing lactose or galactose in minimum percentages of fifteen and twenty, respectively, the development of tetanic manifestations could be definitely prevented. The amount of lactose required was found also to vary directly in relation to the diet protein (casein) content. Of interest also, is the fact noted that no effect was observed from the parenteral administration of lactose or galactose, which indicates that the site of action is probably the alimentary tract. It is possible, in view of this, that lactose may exert its effect through

the development of acidophilic changes in the intestinal flora. However, this may not represent the actual or complete mechanism, as tetany was not found to be inhibited by the ingestion of dextrin which is known to produce acidophilic changes similar to those of lactose.

RAPHAEL, Ann Arbor, Mich.

THE DEVELOPMENT OF THE CEREBELLUM IN THE FROG (HYLA REGILLA) IN RELATION TO THE VESTIBULAR AND LATERAL-LINE SYSTEMS. O. LARSELL, J. Comp. Neurol. **39**:249-289 (Oct. 15) 1925.

The development of the anuran cerebellum is compared with that of urodeles as previously described by Herrick in the ARCHIVES OF NEUROLOGY AND PSYCHIATRY (**11**:621 [June] 1924). The histories are closely parallel up to the metamorphosis of the frog, at which time the lateral-line component disappears. The nucleus cerebelli and the nucleus vestibularis are genetically related and in early stages show considerable similarity of connections which later become modified. The cell pattern of the region from which these nuclei are developed is very simple in the early tadpole. Relatively large cells send dendritic processes laterally which come into relation with several tracts, recalling the condition in the oblongata of *Amblystoma*. This condition persists in the adult to some extent in the eminentia ventralis. At metamorphosis the changes in the fiber tracts of the cerebellum are correlated with a change in the physiologic dominance of the lateral-line system in the larva to preponderance of control by spinal, vestibular and optic systems in the adult.

HERRICK, Chicago.

CYSTS OF THE CAUDA EQUINA WITH DISCUSSION OF CEREBRAL AND SPINAL SUBARACHNOID HEMORRHAGES. S. GOLDFLAM, Deutsche Ztschr. f. Nervenh. **85**:47 (March) 1925.

Cases of spontaneous cerebral subarachnoid hemorrhage frequently contain a history of preexisting migraine. The vasomotor component of the migrainous attack is a causative factor in many cases of spontaneous cerebral subarachnoid hemorrhage; these are frequently neurogenic, diapedesis hemorrhages. Spontaneous spinal subarachnoid hemorrhages are usually of unknown origin, but may occur on a neurogenic basis. A combined subarachnoid hemorrhage in the two locations can occur. Such a case is reported by the author. Another case was observed in which recurrent spontaneous subarachnoid hemorrhages in the sacral region were noted. Many years later a cyst of the cauda equina was found, which was successfully removed at operation. The clinical result was unsatisfactory because of marked arachnoid perineuritis in the sacral region.

HAMMES, St. Paul.

Society Transactions

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

Regular Meeting, Dec. 17, 1925

WILLIAM HEALY, M.D., *President, in the Chair*

CLINICAL AND AUTOPSY FINDINGS IN A CASE OF BRAIN TUMOR WITH UNUSUAL SYMPTOMS. DR. F. A. TOWER.

December 24, 1924, a clergyman, aged 46, was admitted to the McLean Hospital with the following history. His father had had a limited education, but was fairly successful in business and had had one "nervous breakdown." His mother was said to be of a nervous temperament. There was nothing else of significance in his ancestry.

Physically he had always been robust. He was graduated from college and theological school. Then at the age of 44, not satisfied with his work in the ministry, he took an advanced course in religious education at the Newton Theological Seminary. He was industrious, over conscientious, an average student, nervous, inclined to worry and slightly irritable and exacting when tired. He had a marked tendency to self-depreciation and possibly a feeling of inferiority. As a pastor he was popular with the older members of his parish but he was unable to hold the interest of the young people to his satisfaction. When completing his studies at the age of 29 he had a "nervous breakdown."

Prodromal period, from May to Aug. 17, 1924: His church was in debt. There were several factions in the congregation and he was unable to harmonize them. He worried about these things and began to be fatigued both physically and mentally. Previous to this time he had delivered his sermons without notes, but in May he found it necessary to use them because he frequently lost the thread of his discourse.

Onset: During his vacation, on Aug. 17, 1924, he attended morning church service in a city six miles from his home, making the trip in his automobile with his son, aged 12. In church he was suddenly seized with an attack of vertigo. He remarked to his son that the building seemed to be swaying as though it would fall. They went out at once. He drove home operating the car correctly, but he had lost his memory for places. At every intersection of the highways he asked his son the proper direction. Not satisfied that his son had directed him properly, he inquired of every passerby. On arriving home he felt faint and went to bed saying, "I don't know just where I am. There is something wrong with me."

Following this his memory gradually improved so that he was able to recall correctly events previous to the episode of August 17. He had a complete amnesia for the events of that day and a partial amnesia for subsequent events. Many times he recognized callers but could not call them by name. September 1 he had an attack of "nervous indigestion," so diagnosed by his physician. After that he had a craving for food in the early morning around 4 o'clock. On September 30, diarrhea developed, lasting several days, which was attended by prostration and a relapse in the mental condition. Again there was a slight

improvement mentally and physically and on October 28 his wife underwent a major operation without harmful effect on his condition. November 12 he had a "faint spell." The physician was summoned, and found him stupid and complaining of distress in his head. After this he was distinctly worse. He would ask the same questions over and over; he lost his way in the house. December 3 he got up in the morning complaining of being weak and tired and was very dull mentally. From this time on he was noticeably worse. He was disoriented for time, not being able to tell the season even when he saw snow on the ground. He failed to recognize familiar scenes when walking outdoors. He would meet his wife in the house many times each day and greet her with great emotion as though he had found her after a long absence. His spontaneous productions narrowed down to a few phrases and questions, often repeated, a sample of which is the following: "I have just waked up in the past few minutes; all the past is blank."

On admission to the hospital he had a normal appearance and responded to questions promptly and relevantly with good phraseology. An interview demonstrated complete disorientation except for his own identity, and amnesia for his trip to the hospital. His spontaneous productions were few, such as, "What place is this?" "Please tell me where my room is." "How long have I been here?" "This is a complete nervous breakdown, isn't it?" "Will I get better?" and the phrase used at home. He showed emotion when referring to his condition and said he was depressed when asked the direct question. At other times depressive affect was absent.

Subsequent interviews brought out the following regarding his memory. He recalled a few major events since the episode of August 17. When urged by repeated question he did better. His memory for events previous to August and the main facts of his life was good. His own biography checked accurately with the statement of his wife. Confusion and thinking difficulty, other than that caused by the amnesia, could not be demonstrated. Ordinary tests for confusion showed none. No delusions or hallucinations could be elicited. Recent memory continued to be poor. He was unable to remember anything told him during conversation more than five minutes. He did succeed in retaining the names of one physician and one patient and usually named them correctly when he met them. Repeated physical examinations showed nothing abnormal until January 25, 1925. While he was in the act of dressing that morning he was heard by the nurse moaning and groaning. When the nurse entered his room he was found lying on the floor. Questioned by the nurse he complained of headache. Examination by the physician a little later showed nothing abnormal objectively. On succeeding days he was noted to be walking stiffly at times. On January 31 when called for breakfast at 6:55 a. m. he was found partially dressed but unable to go to the dining room. He suddenly fell, became rigid and did not respond to voice or touch. In an instant he relaxed and stood up with the help of the nurse, then settled back into the arms of the nurse. He was incontinent of urine and feces at this time. He was cyanotic and perspired profusely. The temperature was 97.2 F.; pulse rate, 45, and respiration, 18. Seen at once by the physician, he was still stupid and irresponsive to questions. Examination showed nothing abnormal neurologically. About 8 a. m. he answered questions slowly. During the whole day he was confused and stupid, and rambled in his talk. On February 3 signs of organic nerve involvement were first demonstrated. The left abducens was weak; there was a nystagmoid movement of the left eye at the end of excursion to the left. The pupils were normal. Vision in the left eye was better than in the right.

There was no hemianopia and no diplopia. The left abdominal and cremasteric reflexes were absent. The examination revealed no other abnormalities. On February 5 the pupils were unequal; the right was larger than the left; both reacted to light and in accommodation. The left abducens was the same as on February 3. Excursion of the right eye to the left was impaired. Excursion of the right eye upward was impaired, with ptosis of the right eyelid. The left cremasteric reflex was present on this date. The eye grounds were normal at every examination. Mentally, the patient was more sluggish.

On February 7 an outside consultant saw him. Epidemic encephalitis could not be ruled out, and lumbar puncture was done. The pressure of the fluid was equal to 300 mm. of mercury. The fluid was clear. The cell count was 42 per cubic millimeter. The globulin was not increased. The trichloracetic acid test showed double normal. The sugar content was 80 mg. The patient did not have diabetes, as the fasting blood sugar content December 31 was 93 mg.

He continued in bed from February 6, during which time he complained of violent headache when aroused; he became more stupid and confused. He died at 7:50 a. m., Feb. 8, 1925. Necropsy was performed one hour after death. Gross examination of the brain revealed a new growth invading the brain tissue beneath the right lateral ventricle and nearly filling it in its posterior two-thirds. The tumor invaded the brain tissue to within 1.5 cm. of the base of the temporal lobe. Its lateral extent was 2 cm., and it did not extend toward the lateral surface of the cerebrum beyond the plane of the lateral ventricle.

Dr. Percival Bailey examined the new growth microscopically and according to his nomenclature it was an astroblastoma in the group of gliomas.

DISCUSSION

Dr. E. W. Taylor: Was the lesion on the right or left side?

Dr. F. A. Tower: It was on the right side.

Dr. E. W. Taylor: I do not see how it would be possible to make a diagnosis of brain tumor in this case with no optic nerve changes and no headache until the very end. A diagnosis of brain tumor would be nothing more than a shrewd guess unless one could determine, possibly from the spinal fluid examination, evidence of increased intracranial pressure. The only organic sign I think Dr. Tower mentioned was a paralysis of one of the external rectus muscles. The paralysis of the sixth nerve, on account of its long course, may be due to pressure anywhere within the cranial cavity and, hence, is of very little diagnostic value from a localizing standpoint.

Dr. Donald Gregg: In the necropsy report you did not mention the arterial findings. Were they entirely negative?

Dr. F. A. Tower: Yes.

Dr. O. J. Raeder: Was it a single lesion?

Dr. F. A. Tower: Yes.

Dr. O. J. Raeder: Were there any hemorrhages that might have caused a local temporary pressure?

Dr. F. A. Tower: No.

Dr. Morton Prince: Was there any effusion into the ventricles?

Dr. F. A. Tower: The pressure when lumbar puncture was made was 300 mm. of mercury.

DR. MABEL ORDWAY: Had it been possible to diagnose, would any operation have been of value?

DR. F. A. TOWER: It was an inoperable case, since it lay deep in the substance of the temporal lobe.

DR. FRANK FREMONT-SMITH: Did I understand that the protein in the spinal fluid was increased?

DR. F. A. TOWER: Yes, about doubled.

DR. FRANK FREMONT-SMITH: We have been examining both ventricular and lumbar fluid in brain tumor cases at the Massachusetts General Hospital. In tumors lying above the tentorium the protein content is usually normal in both these fluids, with the notable exception of tumors which invade the lateral or third ventricle; in such cases the protein has been found high in both lumbar and ventricular fluid. The case under discussion would fit into this group. A high spinal fluid pressure rarely occurs in epidemic encephalitis.

DR. D. J. MACPHERSON: The question might be raised whether a study of this case would be enlightening to the theory of cerebral localization. In one such study of a tumor involving the third ventricle, I found it simple to list the structures involved but could find no normal physiology to correlate with the anatomic findings. The degree of injury from edema and pressure at a distance was impossible to estimate. It is also a fact that normal axis-cylinders traverse a glioma and are probably capable of function even though lacking a myelin sheath. In my opinion, these considerations make tumors of relatively little value as a type of injury from which one may draw conclusions as to cerebral function from correlation of lesions and symptoms.

DR. F. A. TOWER: This case runs true to form, as tumors in the so-called silent areas of the brain generally do not show organic symptoms until pressure has developed. These are the cases in which we generally get mental symptoms appearing early, but the particular symptoms this man showed are not the ones we generally see. We usually get sluggish mentality which affects the alertness of the patient, and in this case the memory defect was the most pronounced symptom. The episodes which he showed are common in all types of organic conditions in the brain. Should we consider the history to January 25, when his first real cerebral insult was observed at the hospital, we can easily make a good case of manic-depressive psychosis based on his ancestry, his previous nervous breakdown, his over-conscientiousness and worry bringing on fatigue over a difficult situation in his parish, and, of course, confusion which is quite apt to be present in depressions, although not necessarily of the episodic kind that he showed. But we see confusion so many times at the high levels that it is sometimes difficult to eliminate it entirely and say it is not present. When we consider the memory defect we see that his remote memory was very good, even until late in his residence at the hospital. He gave us a very good account of his past life; he did not show the sluggishness we usually get; his replies were good, always relevant, but his recent memory was poor at all times, and he was able to retain only a few facts since the acute onset on Aug. 7, 1924; we have, therefore, recent memory defect with fairly good remote memory. We find that condition most frequently in senile psychoses, but not usually in brain tumor cases. I should like to ask these questions. It first occurred to me that possibly this memory defect was so clear-cut that we might be able to get some definite evidence, for instance, from studying the tract degenerations with serial sections of the brain. Then without considering the fact that senile psychoses concern diffuse lesions throughout the brain, and

knowing, as we do from the examination of many cases since the war, that sharply localized lesions do not give much evidence for definite localization of the higher intellectual functions, study of tract degeneration did not seem a profitable procedure. I leave that as a question; in other words, was it the particular location of the tumor that caused this particular defect? Of course, we have to consider the remote effects of pressure which was not apparent in this case until very late. Generally, when we have pressure we get definite organic signs, but this memory defect appeared months before organic signs appeared. Are we dealing with a toxin in these cases? Is it the toxin that produces this particular effect in which the patient still has the capacity to bring out knowledge which has been stored, but is unable to store accurately and recall that which has come since the onset of the trouble?

GLIOMA AS AN ANOMALY OF DEVELOPMENT. DR. DONALD J. MACPHERSON.

The conception of glioma arising on the basis of maldevelopment has been held by previous investigators who have cited the presence of ependymal cysts occurring in glioma as evidence and discussed the possibility of glial cells changing to ependymal cells and vice versa. Further, multiple gliomas and the occurrence of subependymal proliferation of glial tissue have been noted. The theoretical probability of islands of cells with an abnormal potentiality for growth being isolated at an early stage of development and later from some new stimulus to growth, or the disappearance of inhibition developing as a tumor, have been considered.

In four cases of cerebellar glioma and one mixed tumor (consisting of glial tissue, ependymal cells, cells typical of the neurinomas and ganglion cells) growing in the region of the third ventricle, blocks were taken from the prefrontal, frontal, motor, sensory, temporal and occipital cortex, and from the region bordering the ventricles, and serial sections were studied to note the condition of the glia.

Lantern slides show subependymal proliferation of cells and fiber glia, more especially near the ventricles, but in one case occurring as a small nodule in the cortex of the temporal lobe. These abnormalities of glial growth occurring far from the main tumor were found in every case studied. They were held to indicate that in brains in which a glioma has developed there is evidence of a general abnormality in the glia, more especially in the region near the ventricles. There was nothing in the sections studied to indicate whether these were the result of a congenital abnormality, of stimuli increasing the formative activity of cells or of the removal of hindrances to growth. The occurrence near the ventricles in the line from which growth develops in the embryonal periods, and the occurrence of mixed tissue arising from glia in one of the tumors, were considered suggestive of the possibility of developmental anomalies playing a factor in the origin of tumors arising from glia.

DISCUSSION

DR. H. R. VIETS: It is interesting that Dr. MacPherson should have taken cases of cerebellar gliomas to study because, clinically, two things stand out in regard to these tumors—they are most often seen in young people and, as Dr. Cushing has shown, patients with cerebellar gliomas live longer and do better than patients with tumors in any other part of the brain. Cases of this type in which operation was performed eight or ten years before have been shown us. If these clinical facts are true, it is not easily explained why these secondary

growths that Dr. MacPherson has demonstrated in his cerebellar cases did not develop into tumors.

Dr. O. J. Raeder: I want to ask Dr. MacPherson if he noticed any abnormalities or changes in the nerve tissues other than in the central nervous system, in the sympathetic ganglia, for instance, or in the suprarenal or neural hypophysis? Also, if he feels that the glial cell reaction he showed in the lantern slides is microglial proliferation, possibly a reaction to the tumor growth?

Dr. E. W. Taylor: If it is true, as Dr. Viets and Dr. MacPherson suggested, that all these brains are anomalous, that the glia is abnormal throughout the brain and that there are these separate foci, is it not extraordinary that we so seldom have multiple gliomas?

Dr. Donald Gregg: Most of the cases which you have shown were, I understand, tumors of the cerebellum which also showed reactions or abnormal conditions in the cerebrum. Did the single case of tumor in the cerebrum, which you showed, disclose an abnormal situation in the cerebellum?

Dr. Frank Fremont-Smith: In cerebellar glioma there is almost always some degree of internal hydrocephalus. Is it possible that the lesions described, mostly close to the ventricular wall, were secondary to the hydrocephalus? Might not such careful study as has been applied to these cases reveal similar lesions near the ventricle in cases of hydrocephalus due to acoustic neuroma or cerebellar abscess?

Dr. Donald J. MacPherson: Cases presenting a cerebellar tumor were chosen in order to get the actual lesion as far away from the cerebrum as possible. Patients with cerebellar gliomas are apt to live long, thus, perhaps, giving these small areas time to develop.

Dr. Raeder brought up the question of involvement in other parts of the central nervous system. Unfortunately, in the cases I had, the brain was the only part of the body which had been saved, and no records of the necropsies were available.

Dr. Taylor asked why such foci do not more frequently form multiple gliomas. I do not know. There are a number of cases in which in conjunction with one tumor we see another tumor with a small area of tumor tissue between, and an occasional case with multiple tumors with no question of metastasis. One has no conception of the rapidity with which these small foci are growing. If the primary tumor had been taken out and the patient had lived from six to ten years longer, some of these foci might have developed into true tumors. All of these patients died without operation, so their period of life was probably much shorter than that in a case with successful operation.

Dr. Fremont-Smith mentioned cases of hydrocephalus associated with neuroma. Neuromas are considered by many to originate as developmental anomalies, and it is improbable that the glial changes in the cases I have reported were in any way the result of the hydrocephalus. The more common findings in brains with a hydrocephalus without tumor have been increase in the glia surrounding the ventricle, and granular ependymitis. The growth of the glia takes place away from the ventricle, while in these cases the glial changes were in the subventricular tissue and growing toward the ventricle.

Repersonalization or What Is Hypnosis? Dr. Morton Prince.

The terms hypnotism and hypnosis have acquired unfortunate implications and connotations and are not free from stigma and prejudice even in the minds

of physicians. In the minds of lay people they border on the occult. Some new term is therefore desirable, one that will correctly define the phenomena. There is a general misunderstanding of the nature of hypnosis leading to many foolish questions, as, "How many persons can be hypnotized?" This question, as do many others, indicates a misunderstanding of the phenomena, such as the belief that there is a definite specific state constituting hypnosis. The states of hypnosis are as varied and multiform as there are possible combinations of the psychologic and physiologic components of personality.

But there are certain general principles to which every state conforms. These are dissociation, inhibition and synthesis or reintegration. It is generally agreed that every hypnotic state involves dissociation and inhibition, but it is not so generally realized that it also involves reintegration, with a total result of repersonalization.

By dissociation and inhibition certain mental processes are repressed or prevented from entering the content of consciousness of the moment and certain physiologic processes, such as sensory and motor functions, may also be excluded from the organized personality, resulting in anesthesia and paralysis. By synthesis there is a reintegration of the conscious processes by which dormant systems of thought (memories, etc.) are reintegrated as the content of consciousness. In this way there is a depersonalization and repersonalization of the personality.

Dissociation and inhibition may be of all degrees and kinds, simple or complex. They may comprehend every variety of mental and physiologic component of the mind-body (personality). The same is true of synthesis. All three are normal processes and are absolutely essential for the normal functioning of the mind. The normal states of abstraction, revery and "brown study" are the product of these three processes and are identical in every way with the stage of light hypnosis. Light hypnosis, the stage to which the great majority of subjects are hypnotized, is nothing more nor less than abstraction. Any physician, therefore, who uses abstraction for the purposes of psychanalysis or suggestion, therapeutics, or the recovery of memories, etc., uses hypnosis. It follows that as every one can go into a state of abstraction, every one can be hynotized to this degree. The extreme stages of hypnosis, such as somnambulism, are more rare and are the resultant only of extreme repersonalization brought about by only very extreme dissociation, inhibition and reintegration.

The mental and physiologic constituents of the lighter (abstraction) and deeper (somnambulistic) types were then described showing what phenomena represented dissociation and inhibition and what reintegration, and the type of repersonalization resulting.

Dissociation and inhibition might predominate or it might be synthesis, or both might be in equal proportions. As a result of the two former the field of consciousness may be so retracted as to be limited to a single idea or group of images or memories which alone occupy the field of attention.

Then we have "mono-ideism," so-called. In the extreme types of somnambulism every sort of mental and physiologic dissociation as well as reintegration may be observed. The respective phenomena include the sensory and motor functions, mental traits, the emotions, instincts, etc. These extreme repersonalizations are identical in every way with those of dual personality.

(The part played by external suggestion and auto-suggestion was discussed.)

In view of these principles and the facts of observation the term "repersonalization" is suggested in place of hypnotism. The former correctly char-

acterizes the facts: the latter does not, but expresses an outgrown theory which identified hypnosis with sleep.

This point of view—depersonalization and repersonalization—is important and fruitful in that it allows us, on the one hand, to relate hypnosis to fundamental principles governing the functioning of the mind and, on the other, to class it in a large category of normal states such as abstraction, revery, mystic ecstasy, absentmindedness, emotional crises, etc., and abnormal states, such as hysterical crises, fugues, somnambulism, double personality, etc.

NEW YORK NEUROLOGICAL SOCIETY

Regular Meeting, Jan. 5, 1926

I. Abrahamson, M.D., *President, in the Chair*

A Case of Tuberculose en Plaque with Pathologic Specimen. Dr. Irving H. Pardee and Dr. Leila C. Knox (by invitation).

The case is that of a woman, aged 25, who complained of attacks of a peculiar feeling of tension pain and tonic spasm in the right arm. This was usually accompanied by considerable psychic unrest, a hysteroid reaction with anxiety, but rarely by loss of consciousness. The attacks were repeated at intervals of from two to three days, or once a month. During the first period of observation, five years ago, she showed on examination a persistent hyperreflexia on the right side, with once an unquestionable Babinski sign, and rarely a tendency to clonus. The combination of a hysteroid personality with the paucity of neurologic signs precluded a positive opinion, and the patient was discharged from the hospital with the tentative diagnosis of a left cortical tumor. When the patient again came under observation four years later, she showed unmistakable signs of a tumor in the left precentral area, and died a few days afterward.

The brain at necropsy showed a flat tumor-like mass, spreading caudalward from the frontal lobe to the parietal region, onto the mesial surface of the brain, and downward almost to the Sylvian fissure. It appeared to be an infiltrating glioma. Microscopic examination revealed a tuberculoma, with caseation, fibrosis, numerous giant cells and well formed tubercles. It lacked the vascular lesions characteristic of a syphiloma.

This condition is described in the literature—*meningite en plaque tuberculeuse*—and one previous case is reported with findings similar to those here described.

DISCUSSION

Dr. Abrahamson: Were all the attacks ushered in by the tonic contraction of the hand, with the patient holding on to the bedclothing, and unable to release her grip?

Dr. Pardee: I observed a number of the attacks, which were ushered in by a tonic spasm of the right hand. They were practically always preceded by a consciousness on the part of the patient of the fact that something was happening in her arm, sometimes a numbness, sometimes a feeling of tension or some other paresthesia. It finally ended with a definite clonic movement. She was often anxious during the course of the attack and obviously in a state of fear and distress; this attitude at times dominated the organic features of her

condition, so much so that an impression was frequently made that they were typical hysterical attacks. Because of the variability in the reflexes we were willing to postpone the exploratory operation.

DR. ABRAHAMSON: I would like to call attention to the long period, four years, between admissions to the hospital. Did she on the second admission, have all the signs of pyramidal tract involvement, lost abdominal reflexes, Babinski sign, hypertonia, hyperreflexia and paralyses?

DR. PARDEE: On readmission her right side was partially paralyzed, and she was in a very serious state physically. It was hard to make an examination as she was uncooperative; there was, however, a definite increase of reflexes on the right side, but we could not elicit a Babinski sign.

DR. ABRAHAMSON: The specimen shows a very interesting involvement of the cortex, without involvement of the white matter. Is it possible to have no Babinski phenomenon, with loss of abdominal reflexes and hypertonicity in such a lesion? The next point of interest is that the cortical effects were tonic. We are dealing with a tonic disseveration, and in the vast majority of cases, only when the deeper parts are involved does one obtain tonic spasms. I think this case may throw considerable light on the subject, because of the involvement of the cortex without much involvement of the white matter.

PARALYSIS AGITANS AND THE RIGHTING REFLEXES ("STELLREFLEXE" OF MAGNUS-DE KLEIJN). DR. S. BROCK and DR. I. S. WECHSLER.

This communication is preliminary, and we hope to enlarge on it at another occasion. Briefly, it is this: The essential features of paralysis agitans, i. e., the posture and defect in the performance of the so-called "associated and automatic movements" (J. R. Hunt) are losses of a variety of righting reflex.

Parkinson's syndrome is very complicated and tremor is not an essential sign, its absence being fairly common. Rigidity is common and varies in its intensity, but there are unusual cases without it. This paper is not concerned with tremor or rigidity. There are two absolute essentials in the disease: the assumption of a certain well known attitude, and the loss of certain postural adjustments intimately associated with the attitude; these are the "associated and automatic movements." As stressed by Kraus, this posture represents a "dissolution of erectness, and an inability to achieve that particular righting concerned with the erect posture in man." In paralysis agitans man's normal bipedal erectness is being replaced by the abnormal quadripedal posture of the lower animal. So much for the static phase. In festination, retropulsion and lateropulsion we see this same inability to "get set," this loss of righting, when a change from one posture to another is attempted.

As man assumed the erect posture, he elaborated his emotional life, and the righting reflexes became intimately concerned with the motor expressions of emotion. Facial movements of anger, fright, surprise, etc., were correlated with corresponding somatic postural patterns, the latter falling into the category of righting reflexes. Fusion of the latter with the facial expressions of emotion occurred. One might say that facial emotional movements are affective motor expressions of certain righting reflexes which have acquired an emotional component in man. Hence the concomitant lack of emotional expression in paralysis agitans.

The absence of rigidity in certain cases shows that hypertonus cannot be invoked as a cause of the loss of these righting adjustments.

In Magnus' monograph, "Körperstellung," various righting reflexes are defined and described (labyrinthine, optic, neck, body on the head, body on the

body) differentiated by the afferent pathways transmitting the stimulus, and the location of the centers. A righting reflex may be defined as a coordinated movement which tends to restore normal posture from any abnormal deviation imposed on the animal. Such righting adjustments are always present in the walking state, because minute deviations from normal posture are constantly at work. The rôle of the head (with its great sensory receptors) is to be stressed in the initiation of these reflex movements. In general, the centers are in the midbrain and interbrain. Of course, the centers for the optic righting reflex are in the cerebral cortex. Other righting reflexes occur: those initiated by smell, those dependent on psychic processes in the cortex, etc. The actual center for the righting reflex concerned in the maintenance of the erect posture and its allied reflex postural adjustments is unknown. It may be placed in a hypothetic locus in the diencephalon.

DISCUSSION

DR. WALTER M. KRAUS: This subject is one of the most difficult in organic neurology, for it demands a very intimate knowledge of neurophysiology, and of reflexes in the sense of Sherrington rather than in the sense of Hughlings Jackson. Sherrington worked in the direction of building up reflexes from the spinal level; Hughlings Jackson worked on the question of the release of reflexes from lesions of upper levels.

In the matter of tone, Dr. Brock has stated that a transection of the cord will produce flaccidity. He has also emphasized that a section higher up will permit decerebrate rigidity. From purely clinical experience you will recall the effects of the lesions of various suprasegmental ganglia, many of which disturb tone. These include lesions of the globus pallidus, the red nucleus, the substantia nigra and the frontal and temporal lobes. A vast accumulation of experimental data from Sherrington's and other laboratories shows that tone is essentially inhibited above the segmental system, and that it is produced below the segmental system.

Tone, as Sherrington has emphasized, apparently without universally adequate success, is produced in muscles. It is not produced elsewhere. Tone is a myogenic affair, and it is not produced in a tone center in the brain, nor is it produced in a tone center in the spinal cord. It comes in through the afferent roots, flows into the spinal cord, and is then distributed.

I am, furthermore, quite certain that tone does not originate in the labyrinth. If both labyrinths are destroyed in an animal, there is no change in tone. If one labyrinth is destroyed, there is a change in tone in the neck muscles on the same side. It is, however, secondary to a stretching reaction in the neck muscles themselves, and is a postural change in these neck muscles, due to a unilateral postural influence of the labyinth, and not a primary tone change. The head rotation remains even if the sensory cervical roots from the muscles causing the rotation are cut. The influence therefore passes by way of the anterior roots.

The next problem is that of posture. I stated in 1921 and in 1923 that the patterns of the leg postures concerned with the movement of walking in man are spinally determined. There is no question that a careful reading of Magnus shows that he is of the same opinion, that the patterns for the muscular action of the legs in walking are in the spinal cord. In tetrapods the same applies to the arms. The postures are extension and flexion of the leg, and the corresponding ones in the arm. What is the posture of the arm in relation to the posture of decerebrate rigidity? If there is a lesion about or below the midbrain, the posture of decerebrate rigidity results. If there is

a lesion higher than the midbrain, an entirely different posture of the arm results. With this in mind, let us pass to another question, that of erectness. When there is a lesion in the location which produces parkinsonian disease or pseudobulbar palsy, dissolution of erect posture results. The center for the ability to right, to resume the erect posture, which is lost in parkinsonism, is located above the midbrain. This has been observed before, but what has not been observed, and what constitutes the importance of Wechsler and Brock's paper is that this lost reflex is a righting reflex, a "Stellreflex," in the sense of Magnus and de Kleijn.

Elliott Smith ("The Evolution of Man") believes that the recession of smell and the development of sight largely determined the appearance of the primates. In other words, as the olfactory sense diminishes, sight becomes more and more evident. As the eyes come from the side of the head, where they are placed in a rabbit, to the front of the body, there is a change in the optic chiasm. Lower animals have completely crossed optic tracts. As we ascend the scale, the crossing becomes less and less complete. The animal on all fours, who cannot maintain erectness, desires to see more rapidly. Obviously turning is more difficult when on all fours than when erect. Erectness ensues gradually and finds its highest expression in the most highly civilized animal, man.

There is another factor: the posture of the prehensile arm which, as I have described elsewhere, is produced by ventral muscles, and is placed above the midbrain. At about the same level, supramesencephalic, I have placed the center for erectness. The gradual development of stereognosis in fore limbs (hands) and eyes requires a new receptive nucleus on the afferent side, and this must lie in the region of the thalamus. It is about this region on the motor side in which I have placed the two centers for prehensile arm and erectness, the latter being diseased in parkinsonism. These motor centers correspond to the new sensory stations mentioned.

This brings up still another and a very important aspect of the paper of Wechsler and Brock—the neurobiotactic. In lower animals the center for standing lies below the midbrain. In man it lies above. Something has caused it to appear at a higher level in man. We also know that the center for extension of the legs lies prespinally in man and apes and intraspinally in lower animals. Therefore, it also has moved cephalad in apes and man. This later reflex produces leg extension; the reflex at the bottom of erectness has as its main function extension of the trunk on the legs. It seems to have been drawn cephalad in man. Why should a center for stereotyped posture be located so high above the spinal cord? What neurobiotactic influence is at work? I believe it is the new type of vision and its result, complete erectness. Drs. Brock and Wechsler have described as a righting reflex one which exists at a higher level than those described by Magnus and de Kleijn. They have described the dissolution of erectness. I have attempted to outline some factors which have contributed to erectness and to explain why its centers exist supramesencephalically.

Dr. Brock has described the disappearance of a righting reflex which has to do with stereotyped posture. He has not mentioned the righting reflexes which we all know exist at very much higher levels, reflexes having to do with destereotyped postures. This much is true; if you take your sons to learn ice-skating, as I did a few days ago, you will find that they have a great deal of difficulty in righting themselves. Such righting reflexes are not of stereotyped postures. Their absence does not fit any of the postures one sees

in organic disease, and they must have centers very much higher than those which Dr. Brock described.

Dr. Smith Ely Jelliffe: I do not think what Dr. Kraus has said is all true, but I will confine myself to the remarks of Dr. Brock. It is very pleasing to get this short review of the Magnus-de Kleijn-Rademaker studies; but we could spend many days, if not many weeks, discussing it. There are scores of intricate mechanisms, playing backward and forward, and not a single mechanism, as Dr. Brock would seem to indicate. The way Dr. Brock speaks of paralysis agitans brings up the question of what he means by it. It is not a complicated thing at all from this series of observations. Dr. Brock speaks of it as an "isness" with one mechanism. As a matter of fact, what may be called "paralysis agitans" is a series of syndromes associated with involvement of the mesencephalic, diencephalic and related structures. In that sense there is no such thing as paralysis agitans. It is a mosaic with shifting proportions as the lesions extend to the left or to the right, or further cephalad or caudad. Dr. Brock's summary of Rademaker's paper is quite naive, and I doubt if the author would recognize it. Rademaker's thesis occupies nearly 400 pages in Dutch which fortunately has just been translated into German so that we can all read it. I think Dr. Brock has over-simplified an extremely complicated situation.

Dr. Wechsler: I am grateful to Dr. Kraus for his discussion. It is only since I became interested in this subject that I have begun to understand his work. It seems to me that he has given an excellent contribution to the subject of posture. The contribution of tonight is an attempt to interpret a clinical observation in terms of physiology. I agree of course with Dr. Jelliffe that the question is not so simple, but we are merely trying to apply one physiologic fact to a single clinical observation. Of course, paralysis agitans is a disease characterized by a variety of manifestations. The question is, can we dissociate it into its component parts. We do know that paralysis is not an essential component. We know further that tremor is not always present. We also know that hypertonus is not essential, although it is generally present. What characterizes paralysis agitans is posture or attitude. It is something against which paralysis agitans is always silhouetted. Without going further into the question of tonus, is this posture the result of loss of the "Stellreflex?" This is the central point raised tonight. The man with paralysis agitans cannot quickly resume or assume his normal posture, that is, he cannot right himself. We know, for example, that the "Stellreflex" and the erect posture are influenced by vision; so we tried to find out what happens if you shut the eyes of a patient with paralysis agitans. In a few cases the propulsion was aggravated; in a few others it was elicited when otherwise it was absent. The clinical observation of von Sarbo—according to which, if the patient's head is raised and his vision again shut out, he falls back—is also in line with our observation. The Souques experiment of putting a patient with paralysis agitans in a chair and suddenly throwing him back, may also point to a loss of the "Stellreflex." Our contribution, then, deals with the attempt to show that the loss of the righting reflex is the essence of paralysis agitans. We have left out the neck and labyrinthine reflexes, although in another paper we considered their application in various diseases. In connection with the demonstration which Dr. Brock made with the rabbit I may mention the case of Stenvers. When the patient's pelvis was rotated the head followed every time in the direction of turning. The rabbit, which has its "Stellreflex," you noticed, kept its head in position even though

the pelvis was rotated more than 180 degrees. To state the problem: Is the disturbed posture the essence of paralysis agitans? Is this essentially a disturbance of the "Stellreflex," and finally, is it the result of a lesion in the region just above the midbrain?

THE RÔLE OF ANXIETY IN THE ECONOMY OF MENTAL LIFE. DR. ALBERT POLON (by invitation).

In this paper, anxiety, as a central problem of psychopathology, was dealt with essentially in the light of a psychologic approach. In an attempt to describe and delimit the phenomenon of anxiety it was differentiated on the one hand from the instinctive reactions of fear, a normal self-preservative mechanism, and on the other hand from morbid fears or phobias which should be regarded as inadequate means of anchoring or overcoming anxiety.

Anxiety was defined as a state of demoralization which is invariably induced when the organism is confronted by an overwhelming stimulus. A stimulus proves to be overwhelming when the organism lacks either phylogenetic or ontogenetic equipment to dispose of it in such a manner that the eventual results would be the avoidance of pain or the acquisition of pleasure. In anxiety the pain-pleasure orientation is lost. The consequence is an intolerable state of tension which constitutes a dynamic drive calling for new integrations of the psychic apparatus.

The development of the ego from its simplest to its highest forms may be regarded as occurring under the proddings of anxiety. The moment of greatest helplessness and inability to mobilize adequate responses for survival is obviously at birth. At this low level of the ego, its inadequacy must necessarily be compensated for by the love and care available from the environment. The failure to receive this compensation consistently induces states of demoralization or anxiety to which childhood and particularly early childhood is so prone.

In the course of natural events, when the child is compelled to forego the props and assistance it has heretofore received from the persons concerned with its care it is compelled to evolve a new mechanism which will enable it to get along without external assistance. This mechanism, discovered by Freud, is the mechanism of identification. From now on, the child will behave as if it were one or many persons who played a rôle in its upbringing. The external prop has been shifted inwardly. It is patent that in this state of identification, the personality of the child represents an aggregate of many incongruous elements devoid of unity, or that which we call individuality. The test of experience proves before long that a person whose behavior is dictated by various identification images, which are usually anachronistic, cannot function properly. He does not do this or that because it would further the interests of his personality as a whole, but rather plays into the hands of one or another identification image, which at one time was a source of love and care for him. Clearly this inadequate conglomeration of incongruous elements must give way to a newer integration, or else anxiety is induced.

The new mechanism is that of ego-ideal formation, which comes to the fore when the separate identification images are deprived of their autonomy and are fused, modified or discarded in the service of evolving the uniqueness of individuality.

In tracing the development of the ego, the following stages have been noted: (1) the inception of the ego which must be dependent on libido or else anxiety results; (2) when the libido is being withdrawn, the ego compensates itself

for the loss of its external sources of libido by way of the identification mechanism again, in order to obviate anxiety; (3) when later on this aggregate of identification images cannot function properly, anxiety results, and a newer and higher mechanism must be evolved which would bring about a greater integration and uniqueness. In other words, an ego-ideal is formed on which is conditioned a firm emotional tone of the personality and its greater independence of the outer world. So much for the rôle of anxiety as the push and pressure behind the development of the ego.

The same dynamic rôle of anxiety is found in the evolution of man's love life. From sheer physical gratification, which in the man marks the beginning of life, there eventually comes about the complex consummation of man's sex energy: (1) by way of a normal love life in the service of procreation and accompanied by psychologic superstructure of love; (2) by sublimation of the sex energy, and (3) by reaction formation.

When any of these regular mechanisms of ego and libido development cannot assert themselves, anxiety invariably follows. All sorts of psychopathologic mechanisms then come to the fore, which mechanisms stand for an arrangement that operated at an earlier level. In other words, since the organism cannot take a step forward, it is compelled to regress. The regression takes place in order to anchor or prevent anxiety. Symptoms, then, as well as normal function, are means of overcoming states of demoralization.

The dynamic mainspring of normal ego and libido development as well as of psychopathologic mechanisms is anxiety.

DISCUSSION

DR. A. A. BRILL: Dr. Polon's paper is perhaps one of the best résumés of Freud's concept of anxiety. Dr. Polon begins with anxiety as presented by Freud as an entity separated from other psychoneurotic disturbances, and goes through its whole evolution as observed in the various forms of anxiety and melancholia and in its identifications as described by Freud in "The Ego and the It." In an earlier work (Beyond the Pleasure Principle) Freud discusses anxiety following the experiences gained in the World War with so-called shell-shocked patients who manifested various disturbances of anxiety, and formulates his very fascinating ideas about the repetition compulsion and the two impulses, the erotic and the sadistic. This work laid the foundation for "The Ego and the It" in which the ego with its modifications and identifications is fully developed. However, those who are not conversant with these works may not realize the part that the sexual functions play in anxiety, as Dr. Polon was forced to give mere abstractions of the theories without going into concrete clinical cases. I might mention a case that I recently reported to illustrate some of the identification mechanisms in relation to anxiety. I refer to a woman who herself was an only child and very narcissistic in make-up. She married late in life and had an only child, a boy, aged 13. From what I could gather she lived through her whole narcissism in this boy. She was not at all attached to her husband, but centered all her affection in this child. She guarded him at the age of 12 just as she did when he was 2 or 3; she would not let him play in the street, and when he went out alone she would always warn him to be particularly careful on crossing the streets. Following his death the mother merged into an agitated state of anxiety which lasted for a number of weeks. Gradually, however, she got over it but retained a mixed neurotic condition characterized by definite phobias and obsessions. I will not go into details of the case, but I will just mention the principal

phobia which was an inability to go out alone in the street and particularly to cross streets. Someone had to be with her, otherwise it was impossible for her to go out, or cross a street. In brief, in order to resign herself to this terrible situation of the loss of her son, she identified herself with the lost object and then lived just as she always wished that he would live. She acted like the guarded affectionate love object. If you will recall Dr. Polon's paper, you will clearly see the paths followed by the libido in its conversion into anxiety. At first the anxiety floated freely; she was just agitated and anxious, but gradually the anxiety was, so to say, bound up into the phobia. It would seem that Dr. Polon stresses too much the factor of anxiety, that many of the mechanisms he mentioned are in themselves just as important as anxiety, but this, I feel, is only apparent, inasmuch as Dr. Polon could not give clinical material in the time allotted to him. It is my feeling that in order to understand the problems of the neuroses in all their phases, and some of the psychotic conditions such as melancholia, it is absolutely necessary to follow the paths of anxiety from birth until culmination in pathologic symptoms.

DR. JELLIFFE: Dr. Polon has been valiant and has marched right into the center of things; he has taken clinical phenomena he has seen, and with all the help of his own ingenuity and the material from observations of other people working on the same problems, he attempts, in a way, to dissect the phenomenon under discussion. I feel quite sure that he entertains no illusions whatever, that he has analyzed the entire situation of "Angst." In the first place, I am not quite certain yet as to the suggestion or thought that it is possible by any known process whatever to, as it were, get entirely within the self, and to lose all association with the external world. The external world and self have been inextricably bound up in life ever since life began. Indeed, life depends entirely on the energy of the environment. To make a schism of the kind suggested and have life continue would be impossible. At the same time it is evident that "panic" must in some degree, at least, be concerned with this threatening of the *Id* (das Es).

Secondly, I am not quite satisfied concerning the formulation that the weaning from the mother's womb constitutes the type of "panic" production possibility. Things have been born from time immemorial. Babies have been born into the world long before we were born, or our fathers or mothers. They and their forebears came into the world much in the same way as we did, as apparently a new experience, but not so much of a new experience as may seem on the surface. A recapitulation of the new experiences has been laid down in the pattern, but it is not apparent to me that the individual does have such anxiety with that new birth as might appear from the formula that Dr. Polon has so well given us, in a sense a formula based on Rank's idea of the trauma of birth.

Finally, Dr. Polon's formulation left me a little in doubt as to just where he would group the ego-interest involvements as participants in the panic behavior reaction. If the generally regarded instinct pattern may be said to be made up of ego-interests (self preservation) and libido (race propagation) it does not seem clear to me that the former activities are sufficiently outlined in the presentation. The deeper one descends into the structure of the *Id*, the nearer one comes to physicochemical forces which bind the organism at those levels more closely identified with ego-interests. Panic seems to me to show some of these in process of partial involvement. Whereas we cannot deny libido even to nitrogen or carbon or to gravity, in the deepest meta-

psychologic sense — indeed, as an aside, I might call attention to Matthews' statement that ultimately chemical reaction behavior will need a psychologic formulation — yet, if Dr. Polon is basing his presentation on psychanalytic material, I am as yet unable to allow that such material offers any such insight into chemical behavior, even though I do believe it will ultimately be reached by other methods than those of Pavlov, Cannon, etc. Take the case of angina pectoris and other severe types of cardiac disease: they have been described for us by Corrigan, MacKenzie and Stokes, and these phenomena are not quite as clearly differentiated as they might be from the type of phenomena of which he speaks. There are states for which, as far as I know, he has given us the clinical criteria, which are descriptive of the panic state, and we should have similar clinical criteria for the type of situation which occurs in cardiac disease.

DR. POLON: I agree with Dr. Jelliffe that this presentation is suffering from an excess of schematism, as I understood him to say. However, the justification of this lies in the fact that it is used altogether in the service of furthering lucidity. It is, of course, true that no organ, whether somatic or psychic, ever actually functions apart and independent from the rest of the organism; but for didactic reasons one commonly isolates this or that organ for study. This is indeed an artificial procedure; but that is the nature of all scientific analysis. A given whole is regarded as a composite of elements. Most certainly one must not lose sight of the synthetic qualities of an organism under consideration. But to analyze always means to break up a given phenomenon into its parts and deal with each part as if it were a thing in itself.

As regards anxiety states in such phenomena as angina pectoris and other organic conditions, which I did not mention explicitly, it was nevertheless obviously implied in everything that I said about anxiety. Furthermore, I have indicated that all forms of deprivation, even such as arise within the scope of normal every day life, are provocative of anxiety, and compel the organism to evolve mechanisms to protect itself.

Apropos of Dr. Brill's reference to an apparent absence of emphasis on sex as a factor in anxiety, I would like to say that sex was given its due importance in the causation of anxiety. But since it is the ego aspect of the being which receives the brunt of anxiety, I deemed it advisable to deal with anxiety essentially in relation to the ego. Any more extensive consideration of the rôle of sex in this paper would have made it unsuitable for this sort of a presentation.

RESOLUTIONS REGARDING THE RIGHT OF PHYSICIANS TO TREAT MENTAL CASES IN UNLICENSED INSTITUTIONS. DR. BERNARD SACHS.

Two patients under my observation, who were being treated with superlative care in the past year, in a well equipped unlicensed institution, were ordered removed to a licensed institution by the State Commission in Lunacy. There were no complaints, and no reason for the removal was vouchsafed other than the matter of license. I feel that the patients were unfairly treated, and it is on behalf of the patient chiefly, but also on behalf of the neurologist, that I believe something should be done to change the law so that we may have greater latitude in retaining patients in the unlicensed institution, which to my mind is often better equipped for general treatment than the licensed.

On consulting the attorney general of the state, he upheld the Commission and quoted the law as follows:

Section 59 of the Insanity Law, as amended in 1924, provides: "No person, association or corporation shall establish or keep an institution for the care, custody or treatment of mental disease for compensation or hire, without first obtaining a license therefor from the commission. A patient suffering from mental disease shall not be received and retained for treatment for compensation or hire in any institution for the care and treatment of persons suffering from diseases other than mental. . . . This section shall not apply to a general hospital making provision in a pavilion or special wards for the care, nursing and observation of temporary detention of alleged insane patients, or patients pending commitment to a state hospital or an institution licensed by the state hospital commission. . . . .

These provisions have been enacted because the state wants to know, and the State Hospital Commission is charged with securing, the information as to whether people detained in private institutions are receiving proper treatment, and as to whether their detention is justified."

The attorney general then goes on to state that if the institution has the facilities for the proper treatment of such cases, and is under competent management, as he presumes it must be, there would be no difficulty in securing a license from the State Hospital Commission, and patients could still receive treatment there from individual physicians, subject to the supervision of the physician in charge of the institution.

In a letter which Dr. Haviland, state commissioner, wrote to me in connection with the subject he has made one statement which I will quote: "But it is obvious that no patient who could properly be committed as insane can be legally treated in an unlicensed private institution." My chief objection to this is that the hospital commission has practically the right to say, if we claim that a patient is suffering from a neurosis or a psychoneurosis, that he is insane, and for that reason, he must be taken to a licensed institution. Knowing the progress that has been made in psychiatry, I defy any one to state the exact moment at which a patient is no longer neurotic, but is psychotic, for which reason he must be removed, and cannot be treated in the place where he has been undergoing successful treatment. That is the point which needs distinct amendment. To illustrate this, one of the patients who had to be removed was the daughter of a well known professor in this region, who had had a purulent pulmonary process for a number of years. While she was in that institution, it was necessary to subject her to surgical procedures, and so far as the pulmonary condition goes, the young woman has shown distinct improvement. In the course of the pulmonary disease, she developed a distinct mental aberration. The medical inspector made a diagnosis of dementia praecox, and therefore she had to be removed. To my mind it was from the very beginning a toxic psychosis; however, I am not going to dispute the diagnosis but rather the fact that if one of us has a patient suffering from a toxic process, who in the course of that toxic process develops mental symptoms and we have considered it wise to put him in a properly supervised institution, the moment that institution happens to be visited by an inspector from the hospital commission and the inspector decides the case is one of mental disease, the patient, according to the laws of the state of New York, is taken out of our hands and placed elsewhere. If we allow the law to stand as it is, we are going to get into trouble. Some of us would be inclined, if we cannot treat such a patient and have him under our own supervision in the state of New York, to move him across the border. The laws of Connecticut are much more rational. But be careful

if you do that. You may be accused of spiriting the patient out of the state. Whichever way we try to handle the situation we are going to meet with difficulties, if we allow the law to stand as it is. I am well aware that the hospital commission has the duty to see that patients are not illegally detained. Even if this is a real danger, we should try to amend the law in such a way that the danger can be met. A large class of patients can be treated properly in small institutions where they can receive much more individual care than they do in any licensed institution. The matter is important. I do not wish to speak in a derogatory way of the licensed institutions; they have problems of their own. The question of patients being illegally detained and improperly treated should and must be met. I have seen little of that. I believe the law should be amended for the benefit of patients who wish to be treated in smaller institutions where they can get a great deal more individual treatment, and be under the care of their own physicians; and I do not think that privilege should be denied to the patient or to the physician, although I repeat that the physician is the minor factor in the case. I am going to ask you to take measures to see that the legislature amends the lunacy laws of this state to the effect that it shall be permissible to treat mental cases in unlicensed institutions or at least in such institutions or nursing homes as may be registered under some proper system, but in which the same privilege may be extended to them that is extended to persons suffering from other diseases. It is about time that we should talk about mental diseases in such a way that we are not always faced with this bugaboo of illegal detention. There are unquestionably a large number of patients concerning whom this question cannot possibly be raised, and they should not be compelled to be committed to an asylum or some special state licensed institution. The attorney general says it would be easy for the hospital to which I have referred to obtain a license. I have no doubt it would be easy. That would change the entire character of such a home; and secondly, a licensed institution, according to the definition of the law, must necessarily employ a resident physician, or must have a physician in charge of the home. That at once changes the entire aspect of the situation, for the simple reason that very few nursing homes can afford to engage a physician as sole attending supervisor of a relatively small institution; even if they found some one who was willing to accept that position at a relatively small salary, the general caliber of such a person would not be such that many of us would care to entrust our patients to him. It is a matter for you to decide. I have no personal feelings at all. I appeal to this society either to pass resolutions tonight, or if you do not feel you want to do that, I would suggest that a small committee be appointed to try to formulate some amendment to the law which would make it possible for those suffering from mental disease and from some forms of psychoses to be treated in unlicensed institutions.

DISCUSSION

Dr. F. Peterson was unable to be present, but sent the secretary a letter, most of which follows:

"I suppose that all any good physician desires is the safe and proper care of his patient and the patient's early recovery, no matter what the ailment. . . As time has gone on, the recognition of insanity as a disease and not a legal offense has gained some ground, so that we see a good deal of latitude allowed now in the treatment of many cases of insanity in general hospitals and psychopathic institutions without the traditional legal formularies, and indeed

in many states committed patients are now paroled by the thousands from asylums to their own homes or suitable boarding places. There is a growing tendency to look on insanity as a disease and not a misdemeanor.

Things may be much different now but when I was president of the lunacy commission for several years, our state hospitals were always much overcrowded and the twenty-five private retreats for the insane under my jurisdiction were of varying degree of character. Some were excellent in every respect, while others were quite dreadful places. I had a law passed to give me an inspector on that account. I believe there are several inspectors now. I felt that if we must enforce commitment of these unfortunates to some licensed retreat, we as state officials should be able to guarantee good and efficient care in such legalized sanatoriums. I suppose at this day, eighteen or twenty years later, this good care can be guaranteed in all of the forty or more institutions for the insane in the state. Otherwise, it would be a serious matter for state officials to force patients against their own wills and contrary to the wishes of the family into such legal commitments. At that time I felt that I should not interfere with any mental cases being treated in general hospitals, at a place like the Neurological Institute or at any reputable rest house operated by respectable and trustworthy trained nurses under the care of reputable family physicians or well known specialists. It seemed to me obvious that under such circumstances the best sort of care and treatment were being accorded to patients, and at the time I could not myself guarantee that if committed to some of the licensed places they would have as good and as scientific attention. Of course places were called to my attention where mental cases were being detained and treated without license, and where the personnel in charge and in attendance were without standing in their communities. Such places should naturally be driven out of existence, and this was one of the purposes for which I inaugurated the system of inspectorships. After all, perhaps the chief purpose of a hospital commission of a state may be considered to be a safeguarding of the interests of the insane of the state, the guaranteeing of the most ideal and painstaking care of the insane under their actual jurisdiction, and the intelligent unprejudiced consideratoin of the care of these sick people in general hospitals and unlicensed special hospitals or sanatoriums.

General hospitals throughout the state should be encouraged to open quarters for the reception and study of the supposedly insane pending commitment, so that jails should not be used for detention as is all too frequently the case now in many counties."

Dr. C. Floyd Haviland: I am, of course, in accord with Dr. Sachs in seeking to promote the interests of the patients concerned. However, in dealing with the problem of mental disease, it is necessary to view it from a broad standpoint, and not from the standpoint of a few isolated cases. The magnitude of the problem of mental disease in the state of New York is one of its most striking features, and it would seem necessary to consider average cases and average situations respecting them in attempting to frame statutory provisions covering the matter. The public and private institutions for the care of mental disease now admit approximately 9,500 patients a year, and in the vast majority of instances no hardships result from present statutes. Such cases as cited by Dr. Sachs in no way represent the average case, even among those admitted to private licensed institutions, for even among them the present law does not appear to result in hardship, nor offer obstacles to prompt treatment.

As a matter of fact, I believe the so-called insanity law of the state of New York renders it possible for patients to receive prompt and early treatment as do the laws of no other state, and for such reason I believe that the present insanity law of the state is the best in the country. That there is reason for such belief is shown by the fact that other states are constantly using the insanity law of this state as a model in framing similar legislation; and at present California is attempting to revise its entire code of laws referring to the treatment of mental disease, using as a guide the New York statutes.

The history of "insanity law" in this country shows that at first the idea of custody was paramount, the statutory provisions being principally concerned with the legal procedure leading to ordinary commitment. However, in this state statutory provisions have been enacted supplementing the ordinary method of legal commitment of the so-called insane, whereby proper cases may readily be admitted to either a public or a licensed private institution for mental disease, with a minimum of legal formality. Treatment is now available for all proper cases without the necessity of commitment.

There is, first, provision for voluntary admission of patients to any public or private licensed institution on voluntary application, the only conditions being that the patient shall be in such mental condition as to understand the nature of his act in making application, and that his condition shall be such that treatment in an institution for mental disease is proper and the applicant is willing to agree to abide by the rules of the hospital and to give ten days' notice in writing before leaving.

The second liberal method is the so-called physician's certificate, whereby one physician may make a written statement setting forth his reasons for believing that a patient may be properly received for treatment in either a public or a private institution for mental disease, whereon such patient may be received for an indefinite period, so long as the patient does not object and no person objects on his behalf. If objection is raised either by the patient or some person on his behalf, proceedings must, of course, be taken for commitment or the patient be discharged. However, it would seem that the provision mentioned, together with the voluntary form of admission covers much of the objection raised by Dr. Sachs, rendering it possible, as such methods do, for a physician to arrange for the institutional care and treatment of a patient without hindrance or delay, so long as the physician is willing to utilize either a public or a private licensed institution for mental disease for the purpose.

In addition to the methods of admission mentioned, there is also a provision whereby a health officer may execute a certificate which is valid for a period of thirty days, during which a patient may be kept in a hospital pending commitment. There is also statutory provision for the so-called ten days' emergency admission, which means simply that a patient may be admitted to a proper hospital on the usual medical certificate only, which remains valid for a ten-day period, during which time the usual order of commitment may be obtained. It thus would seem that so far as statutory provisions are concerned, mental patients in this state need not be deprived of prompt institutional care and treatment through any defect of law.

As to the specific point raised by Dr. Sachs respecting unlicensed private institutions to supplement the present private licensed hospitals, I would say that even now mild mental patients may be cared for in unlicensed institutions. The State Hospital Commission has never ruled that the presence of mental

disease as such necessarily means treatment in a licensed institution. The commission has, as it believes, liberally ruled that only such mental patients as may fairly be deemed to be committable are of necessity treated only in licensed sanatoriums. A case comes to my mind of a definitely deteriorated dementia praecox patient, who, however, is quiet and manifests no offensive conduct disorders, so in the judgment of the commission the necessity for the patient's commitment may be regarded as open to question, and hence no objection has been raised to the patient's treatment in an unlicensed institution. However, when the propriety of commitment is clearly indicated, the State Hospital Commission is definitely of the opinion that the patient should receive institutional care only in a private licensed institution or a public institution under the jurisdiction of the commission, that there may be no question but that such a patient who is legally deprived of liberty is placed only in an institution in which proper standards are maintained.

So far as I am aware, there is no difficulty in securing admission of patients to private institutions, as a considerable number of them are rarely filled to capacity. As regards the desirability of placing patients in small institutions of limited capacity, I would say that there are licensed sanatoriums in this state ranging in capacity from two or three to 150 beds or more.

Essentially the licensing system means a method whereby the maintenance of standards can be assured. If the state through process of law subjects a mental patient to institutional treatment, it seems obvious that it is the duty of the state to adopt means to render certain the maintenance of proper standards. Such means would, of course, be lacking, were unlicensed private institutions permitted to receive patients in such mental condition as to warrant commitment.

I would readily admit that the institution mentioned by Dr. Sachs maintains standards equal to those maintained by the licensed institutions, and such a sanatorium would have no difficulty whatever in securing a license. However, unlicensed institutions maintaining such standards are rare, and I venture to assert that for every such unlicensed institution as described by Dr. Sachs, there are at least a dozen unlicensed institutions maintaining much lower standards, in which mental patients could not be expected to receive proper care and treatment.

Apparently the main reason why the sanatorium mentioned by Dr. Sachs has not sought to be licensed is because of the necessity of having a resident physician. However, the State Hospital Commission feels that there should be a resident physician in every institution dealing with such extreme cases of mental disease as to warrant commitment, that there may be a physician on call to meet emergency situations, which as we all know, are apt to occur at any period during the twenty-four hours.

The past experience of the State Hospital Commission indicates that just as soon as vigilance is relaxed, unlicensed institutions for mental diseases are established on a commercial basis, with scant heed to patients' interests and an utter failure to maintain proper standards of treatment. A case in point is that of a chiropractor, who was found some time ago caring for several cases of dementia praecox in a private house on the west side of New York, under most deplorable conditions. There was no medical attendant, and the only caretaker of the patients was an ignorant foreign woman devoid of experience in caring for mental disease. The patients themselves were found in a state of bodily uncleanliness, torn clothing and generally unkempt condition. Their relatives had been willing to consign them to the chiropractor's care, merely because of the low cost, his charge, of course, being

below that of a regular licensed institution. There is scarcely a month that the State Hospital Commission does not receive complaint regarding some unlicensed institution caring for mental patients, and investigation shows that perhaps half of the institutions brought to the commission's attention are illegally caring for patients under improper conditions. If unlicensed institutions are to be authorized by law to care for mental patients, there will then, of course, be no way whereby the state can force the removal of patients from the improper conditions found in the vast majority of such institutions.

There is undeniably a tendency, particularly in the legal profession, to seek greater legal restrictions respecting the institutional care of mental patients. There has, for instance, been a bill introduced into the legislature for the past several years providing for a jury trial as a prerequisite for commitment. Even last year the bill was only defeated after considerable effort. Thus, there appears to be a great danger of an adverse reaction whereby treatment of mental patients will be rendered more difficult if we go too far in removing the state's control of the situation. That such control should be exercised through the continuance of the licensing system for private institutions for mental disease is, I believe, clearly indicated by past experience. If such control should be removed, I am confident that it would be prejudicial to the interests of the vast majority of the patients concerned.

Dr. Carlos F. MacDonald, a former state commissioner in lunacy, by invitation, sent a letter to the secretary which bore out the remarks of Dr. Haviland in the main and was in part as follows:

"When this commission, in the first year of its existence, 1889, began an investigation of the private institutions for the insane in the state of New York, it was found that a considerable number were unlicensed and receiving many manifestly insane persons whose condition was such as to require that they be placed under legal control and supervision — in other words, by commitment to licensed institutions for the insane. These unlicensed institutions, of which there were several, were none of them conducted by persons who were qualified, either by experience or otherwise, to conduct such institutions, the proprietors of several of them being nonmedical persons, both men and women.

It is hardly necessary to say that we found many instances of the grossest abuse in the conduct of these institutions, not to mention instances of ill treatment, and neglect of the inmates; and there were also, among the licensed institutions, several which had received licenses from a former administration, whose proprietors were grossly incompetent to conduct such institutions.

The commission, therefore, after due consideration, proceeded, under statutory provision, to revoke the licenses of all private institutions for the insane, and to issue new licenses to those which were considered worthy. We also issued a general order, requiring that all licensed institutions be conducted by a physician in charge, who had had at least five years' experience in the care and treatment of the insane in an institution for the insane, together with certain qualifications as to professional and moral standing.

It is my opinion, therefore, that the adoption of the proposed resolution would mark a decidedly backward step."

Dr. Thomas William Salmon (by invitation): It seems to me that this involves some quite complex considerations, and is not a question to be settled overnight. If recommendations are made hastily, the society might put itself on record in favor of a change in the law which would not work for the benefit of the patient. Would not the most practical way be for the society

to appoint a small committee to cooperate with the New York Society for Clinical Psychiatry and the New York State Hospital Commission in the preparation of such amendments in the statutes as may be thought necessary?

DR. WILLIAM L. RUSSELL (by invitation): It should be clearly understood that the State Hospital Commission has a very wide latitude in making regulations in regard to institutions. The law does not designate all the requirements that are laid down, such as the qualifications of the physician in charge, and it seems to me it would be very much wiser to take the problem up with the commission and see what can be done about the regulation of licenses. I think any attempt to break down the license system would be unfortunate, and could not be carried through. Every country has some safeguard for people suffering from mental disease. If brought before the legislature, not only the legal aspect, but also popular prejudice will come to the front. We should realize what progress has been made. Instead of all being committed, as was the case when the license system was introduced, a very large proportion of the patients are now admitted on voluntary application. It would not be possible to have a system in which voluntary patients were being taken care of in licensed institutions, and the same class of patients in unlicensed institutions. It seems to me that the wisest plan would be to have a committee appointed for a conference with the State Hospital Commission, to consider if the purposes which Dr. Sachs has in mind, with which we all sympathize in a measure, cannot be accomplished without appeal to the legislature. The time is ripe for a revision of the license system in view of the great change that has taken place in the psychiatric situation.

The president appointed a committee consisting of Drs. Kirby, Peterson and Sachs to consider the question further and to make a report to the society.

SOCIÉTÉ DE NEUROLOGIE DE PARIS

Regular Meeting, Jan. 7, 1926

ANDRÉ LÉRI, M.D., *President, in the Chair*

THE MYASTHENIC FORM OF CHRONIC ENCEPHALITIS; SOME MYASTHENIC SYMPTOMS CONSEQUENT ON EPIDEMIC ENCEPHALITIS. GUILLAIN, ALAJOUANINE and KALT.

The feature with which we are concerned is not merely a question of abnormal fatigability, a common phenomenon in epidemic encephalitis, but one of progressive fatigue or paresis as a result of muscular effort. The myasthenic symptoms may occur in the acute phases or later in the chronic forms, either with or without the parkinsonian syndrome; they may be diffuse or limited to certain groups of muscles. When they affect the muscles innervated by the mesencephalic segment they may simulate rather closely the picture of myasthenia.

Case History.—A man, aged 57, noticed in January, 1925, that he saw double, without other general or local disturbance. The diplopia diminished and became intermittent, but reappeared in October. At this time there was also ptosis, particularly toward evening. Shortly afterward he complained of neuralgic pains in the lumbar and crural regions without fever or somnolence, which obliged him to go to bed. After this episode he noticed an abnormal

fatigability in walking, equally intense in the upper extremities; after walking a few hundred yards the intense fatigue forced him to rest. Now the disorder has spread to the masticatory muscles; during the course of a meal, chewing becomes progressively tiring, so that he can no longer eat bread.

On examination there is noted bilateral ptosis, weakness of the jaw muscles and rapid exhaustion of muscular power in the extremities. The first attempts with the dynamometer give normal readings, but after the third or fourth attempt the needle barely moves. In the second place there is an abortive parkinsonian syndrome, particularly on the right side. The right hand moves less than normal in walking, the right side is somewhat stiff and the expression is somewhat fixed. There is definite tremor of the right hand. Electrical examinations reveal no myasthenic reaction, and no change in chronaxia on repeated effort. There is a slight reduction in chronaxia in the masseters. This points to a lesion of central origin.

We have encountered a similar case in a young man following undoubted acute encephalitis. A few months after the attack there developed a syndrome resembling myasthenia: fatigability of the lower extremities; impossibility during the later part of a meal of continuing to masticate or even to talk; rapid exhaustion of the power of closing the hand.

DISCUSSION

Dr. Froment: In my hands, hyoscine has acted as a great stimulant in these cases; 0.5 mg. injected subcutaneously has produced more effects than 4 mg. of strychnine. I have had less success with scopolamine.

Dr. Babinski: In regard to the possibility of using scopolamine over long periods, I have followed patients who took by mouth from 0.5 to 1.4 mg. of scopolamine hydrobromide almost without interruption for years without ill effects. The reduction in the motor disturbance more than compensated for the disagreeable general effects. Such tolerance may, however, not be constant.

Dr. Sicard: I give my patients the following directions: Try out for a week each of the following medicines: scopolamine, hyoscine, hyoscyamine. Usually scopolamine or hyoscine gives the best results.

Dr. Alquier: Like M. Froment I find that the majority of patients prefer hyoscine to the more depressing scopolamine. It seems to indicate that the two products are different in spite of certain statements. I have given up injections in favor of pills containing 0.1 mg. from two to five of which are taken daily at the patient's convenience. Many patients stand this well, but some manifest sudden crises which are to be combated by digitalis in small doses.

Dr. Sézary: This stimulating action may be brought about by other substances than hyoscine. Extract of suprarenal and of posterior pituitary lobe gave temporary results, but testicular extract gave even superior results.

Dr. Trénel: The diversity of action of hyoscine may be due to sterilization of the product. At a temperature below 100 C. hyoscine becomes transformed into an inactive isomer. Aging of solutions diminishes their potency.

Opacity of the Falx Cerebri (Ossification or Calcification) Demonstrated by Roentgenogram in a Woman Suffering for Ten Years with Progressively Increasing Headache. Guillain and Alajouanine.

This article will be published in full.

PYRAMIDO-OPTOSTRIATE SYNDROME OF ENCEPHALITIC ORIGIN. LAIGNEL-LAVASTINE.

A woman, aged 65, had a series of vasoconstrictor crises of the upper extremity simulating Raynaud's disease. Later there developed difficulty in walking that was considered hysterical. In November there existed four groups of symptoms: choreic movements, predominating in the toes; exaggerated reflexes with plantar extension; noncerebellar ataxia with loss of the sense of position, but preservation of pain, touch and temperature sense, with bizarre sensations of crushing, cold, shivering, crawling and exaggeration of the vasoconstrictor and pilomotor reflexes. Such an association of pyramidal and sympathetic disturbances with choreic and ataxic disorders indicates an involvement of the basal ganglia. Hyperglycorrhachia of 110 mg. without albuminosis or lymphocytosis permits this pyramido-optostriate syndrome to be referred to encephalitis, an attack of which this patient had two and a half years ago. Treatment by intravenous injections of sodium salicylate has been followed by disappearance of the choreic movements, but the other troubles persist.

OPAQUE VERTEBRAE. THEIR DIAGNOSTIC AND PROGNOSTIC SIGNIFICANCE. SICARD, HAGUENAU and LICHTWITZ.

This article will be published later as an original contribution.

STUDIES ON SENSIBILITY AFTER DORSAL RADICULOTOMY FOR CAUSALGIA. SICARD, HAGUENAU and LICHTWITZ.

This article will be published later as an original contribution.

PARKINSONIAN TREMOR IS NOT A TREMOR OF REST. FROMENT and DELORE.

The conception that parkinsonian tremor is one of repose is classic, but this needs examination. What constitutes "repose"? It is a matter of common observation that sleep makes even the most marked tremors disappear. Patients realize that in the instants that precede or follow sleep the tremor is greatly reduced or even absent. Is it not strange that sleep, which is the only phase of complete muscular repose, completely stops a "tremor of rest"? A patient seated, his forearms resting on an arm-chair or a table sees his tremor increase to a maximum, whereas it disappears when he shifts from this attitude which is considered one of repose. But is this an attitude of repose? A traveller at night knows well the fatigue of a sitting position. The parkinsonian patient should be studied under conditions that more nearly approach complete repose. If he supports his body comfortably, stretches out at ease and sinks into a big chair, the tremor is greatly reduced. The tremor of parkinsonism is a function of the static condition, having to do with the whole body. When the necessity for posture is abolished, the tremor ceases. We took an elderly sailor, a great trembler, to a bathing establishment and told him to float, thinking that the tremor would be abolished. To our surprise he showed such a paroxysm of tremor that he almost sank, even though he was a good swimmer. The water was cold, and the man shivered, almost frozen by the cold; the importance of the heat factor was thus brought out. A steam chamber at a temperature of 50 C. was much more conducive to relaxation. A bathtub at 40 C. was substituted, but here it was necessary for the patient to contract some muscles to keep his head out of water, and the tremor increased.

These facts lead to the conclusion that there is no tremor of repose. Tremor reaches its maximum when the body, insufficiently supported, assumes a strained position. It diminishes when the body is completely and comfortably supported.

We advise our patients to rest in this way several times a day. The term "tremor of rest" should be dropped as false, and the term of Klippel and Lhermitte, "static tremor," be substituted. We would prefer "dystatic" to describe this particular form of motor defect.

PARKINSONIAN RIGIDITY AND COGWHEEL PHENOMENON DISAPPEAR DURING REPOSE. THEIR DYSTATIC CHARACTER. FROMENT and GARDÈRE.

To the characteristics of the parkinsonian type of rigidity, as compared with those of pyramidal lesions, must be added the following: Various attitudes of the body bring about changes in the intensity of rigidity and of the cogwheel phenomenon; indeed, they seem to be functions of the static posture of the body. Flexion and extension of the wrist was chosen for study because such a movement does not disturb the general posture of the body. This movement was then carried out first with the patient at complete rest, then supported, finally without support. Complete repose was found to be impossible, even in bed, so that a morris chair was chosen and the patient disposed as comfortably as possible. In this position, resistance to passive movement diminishes greatly. Even myographic and electromyographic studies fail to reveal any muscular response. When the patient lifts his head from the pillow the rigidity in the wrist returns, and is exaggerated when he rises to the sitting or standing position. Myographic and electromyographic studies reveal this difference as well as mere physical examination.

From these observations, carried out on a number of patients, we may conclude that the rigidity and the cogwheel phenomenon exhibited are functions of the static posture of the body in general. In other words, there is in these patients a dystatic condition.

PARADOXIC PARKINSONIAN KINESIS, STRIATAL PARADOXES AND DISTURBANCES OF THE FUNCTION OF STABILIZATION. FROMENT and GARDÈRE.

Souques has called attention, under the name of paradoxic kinesis, to almost miraculous transformations to be observed in parkinsonian states. They are sometimes truly theatrical, as in the case followed for more than twenty years by Souques. This patient could not stand or walk without two assistants, but suddenly, dragging them after him, he ran up stairs two at a time. Another case is that of a young man, in Babinski's service, who could not even sit up in a chair unsupported, yet who would suddenly get up, run about the hall, dance and sing. Such transformations may be quite frequent. It is the rule to find that running, jumping, swimming in warm water and bicycle riding are well carried out by these people. Such phenomena cannot be neglected in the discussion of the mechanism of paralysis agitans.

Jarkowski has given an ingenious explanation of paradoxic kinesis. Each movement is the resultant of the combined action of the affectivomotor center in the striatum and of the directing center in the cortex. Parkinsonian rigidity suggests a reduction of the function of the affectivomotor center and predominance of the directing center. Thus the rigidity may disappear under the stress of an energetic excitation, which compensates by its power for the weakness of the center. But this meets with the objection that the rigidity also disappears at complete rest. We see in parkinsonism a difference between the tonus flexors and extensors, which is shown even in chronaxia readings. This disturbance tends to throw the body out of equilibrium. Equilibrium, however, in man, just as in bicycles and aeroplanes, is the more stable the greater the speed. Hence, during quick movements, equilibrium is better main-

tained than during slow movements. Similarly with the accessory movements of the arms—they give greater ease and speed to walking. But during slow and careful walking as on an icy ridge, or in a child taking its first steps, these movements are abolished; there then comes into play a general stiffening of the body with less tendency to throw it suddenly off its center of gravity. When the balance between the flexors and extensors of the trunk in particular is disturbed, the bodily equilibrium is threatened and consequently the accessory movements are not brought into play. However, as the body gains momentum by increasing the rapidity of the progression, these accessory movements, previously suppressed, come naturally into play.

HYPERTONIC PENDULAR REFLEX. FOIX and JULIEN MARIE.

This patient presents a curiously exaggerated pendular reflex. When the patient is seated the leg does not fall straight, but extends outward at an obtuse angle. When the patellar tendon is percussed there is a brusk reaction, but instead of being inhibited, it continues, sometimes from ten to thirty times, at a rate of 140 to the minute, whereas the ankle clonus of the same patient is at the rate of 400 per minute. This reflex scarcely modifies the electromyogram whereas clonus does so in a characteristic manner. We have observed this in cases of multiple sclerosis and in three cases of thalamic disease with hypertonus. It may also be seen in cases of pyramidal lesion with hypotonus. Evidently the weight of the limb and the hypertonus are the two factors in the condition. It brings to light the dissimilarity in the nature of the rigidity of fixation which tends to immobilize the limb with pyramidal contracture which, constituting a simple increase in muscular tonus, may permit the pendularity to appear.

A CASE OF NYSTAGMUS OF THE PALATE WITH NECROPSY (PRESENTATION OF ANATOMIC SPECIMENS). FOIX and TINEL.

SYLLABIC PALILALIA. MULTIPLE AREAS OF INTRACEREBRAL SCLEROSIS. FOIX and CHAVANY.

Quite frequently surprises await the man who would correlate clinical manifestations with pathologic findings in cases of organic disease of the brain, especially in cases of hemianopia and of aphasia. In such cases there is usually more or less dementia, and the blame is laid on minute alterations in the cerebral cortex. However, these changes sometimes lie in the deeper structures, especially the subcortical white matter.

The patient here presented was a vigorous man, aged 72, who gained the nickname "Dididi" from his speech. He was somewhat demented, but docile, and made a nuisance of himself by using other patients' possessions. He had a curious habit of repeating syllables: "C'est ma jambe qui qui qui qui qui ne vas pas pas pas pas . . . bien ce matin." It was not stuttering, nor was there dysarthria. His trouble seemed closer to aphasia. He became angry easily, and the syllabic palilalia became so pronounced that his meaning became incomprehensible. Writing was impossible. His demented state rendered accurate examination impossible. He managed to help himself in all things.

One might have expected serious cortical and meningeal changes, but at necropsy nothing gross was found. Examination of microscopic sections, however, disclosed numerous sclerotic foci in the subcortical white matter with considerable atrophy, and with dilatation of the ventricles. There was intense multiplication of neuroglia nuclei in the demyelinized foci. The large number of lesions, although small in size, could have interrupted a considerable pro-

portion of the projection fibers in different parts. The condition seemed to be neither infectious nor ischemic, but rather a disintegration analogous with that taking place in the corpus striatum during disintegration: poor nutrition, followed by degeneration of parenchymatous elements and proliferation of neuroglia.

NEUROPSYCHIATRIC SYNDROME IN ALKALINE COLITIS. BEHAGUE and MATHIEU DE FOSSEY.

Three patients with mucous colitis are presented who show various nervous and mental symptoms: exaggeration of superficial and deep reflexes; presence of fascicular contractions like those of paramyoclonus multiplex; periodic tremor of the extremities, of the tongue and of all muscles, with disturbance in movements; difficulties in speech; extrasystoles; persistence of pupillary contraction to light with abolition or diminution of the reaction to distance; sensations of deep, transient aches and physical depression with rapid fatigability. Psychic symptoms are: unrest, anxiety, sadness, despair, slowing of thought; memory disturbance, particularly for proper names and for figures; difficulty in concentration; perfect insight; insomnia during the early morning. The intestinal symptoms are: heaviness in the right iliac fossa; fugitive pains in the colon; loss of appetite, heart-burn, gastric distress; pain on palpation of the right iliac fossa, with cecal gurgling, and spasm of the descending colon. The stools are scybalous or pasty, sometimes soft, of fetid odor and alkaline reaction, with the presence of *Amebae coli* and normal or increased ammonia. The symptoms are relieved by the treating of the digestive disturbance.

THE EMACIATION DYSTROPHY. URECHIA and MIHALESCU.

It is well known that in the course of encephalitides (general paralysis, epidemic encephalitis), in dementia precox, in manic-depressive psychoses, in mental confusions, etc., as well as in other toxic acute diseases, states of obesity or of emaciation may occur. During the course of general paralysis, particularly in its terminal period, extreme emaciation may occur although the patient continues to eat enough. Necropsy in these cases has failed to demonstrate any glandular alteration that might explain this cachexia. In epidemic encephalitis one may occasionally encounter extraordinary emaciation, which no medication can prevent and which continues even though the patients eat well. In two of these cases at necropsy we have found no glandular or organic lesion sufficiently pronounced to explain this emaciation dystrophy. In one of these cases we found tremendous alterations in the periventricular nuclei, and intense alterations in the nucleus supraopticus and nucleus proprius of the tuber cinereum. In the course of catatonia we encounter patients who emaciate enormously without other explanation than a trophic disturbance. The same thing may be observed in manic-depressive psychoses. In hydrocephalus extreme emaciation may be encountered. We also recognize a hypophysial cachexia, in which the emaciation is confined largely to the lower extremities; there are also facial hemiatrophy, and dystrophies that cannot be explained satisfactorily on the basis of an endocrine disorder. Moreover, necropsy in these cases has shown no significant alterations in the hypophysis; sometimes there have been alterations in the tuber cinereum, though rather more often this region has not been examined microscopically. Sclerodermia, in which there is coincidently atrophy of the skin and absorption of the fat tissue, must have close relationship with the nervous system. Irritative changes of

peripheral nerves sometimes show along their course a reduction of adipose tissue.

These nutritive disorders are frequently accompanied by other trophic symptoms, among which may be mentioned edema, cyanosis, dystrophy of the hair, nails, skin, etc. Hypothermia is practically constant. Recently, certain authors, in order to explain this emaciation dystrophy, have invoked the hypothesis of alteration in the vegetative centers.

We have examined the endocrine glands and the nuclei of the tuber cinereum in three cases of emaciation dystrophy, one case of general paralysis and two cases of idiocy (one of them with hydrocephalus). In all, the nuclei of the tuber cinereum showed intense alterations whereas the endocrine glands and other organs showed no lesions of sufficient intensity to explain the status of the patients. We believe, therefore, that emaciation in nervous diseases may be referred to alterations in the tuberal vegetative centers. It is impossible at present to explain the mechanism of this dystrophy or to decide which nuclei are concerned. In the three cases the nuclei periventriculares and suprachiasmatici showed intense changes, but the other nuclei also showed degeneration although less pronounced. The part played by these nuclei in metabolism is little known. New investigations in this direction are necessary both from the physiologic and from the anatomic point of view.

THE CLAUDE BERNARD-HORNER SYNDROME IN MEDULLARY COMPRESSION LOW DOWN. CONOS.

About five years ago I studied a case of Claude Bernard-Horner syndrome with a tumor of the lumbar cord proved at operation and at necropsy. Since then I have seen two more cases:

CASE 1.—Medullary compression at the level of the sixth, seventh and eighth thoracic vertebrae. An operation was performed. Myosis, enophthalmos and narrowing of the palpebral fissure were present. Mydriasis occurred during the last days of life. Death took place but no necropsy was performed.

CASE 2.—Medullary compression between the eleventh thoracic and third lumbar vertebrae. Myosis, enophthalmos and narrowing of the palpebral fissure were present. Improvement occurred during antisyphilitic treatment.

I believe that the Claude Bernard-Horner syndrome has not been reported in medullary compression below the ciliospinal center. However, in two of the three cases in which this occurred, the diagnosis of low medullary compression was proved anatomically; in the third case it is altogether plausible. The existence of the oculosympathetic syndrome in cases of compression in the thoracic or lumbar region is not without practical import since it reduces the value of this syndrome in cases of spinal localization. The pathologic physiology of this phenomenon is not understood. There may be centers in the lower spinal cord acting, either by intramedullary or extramedullary pathways, on the ciliospinal center. There is some evidence that lesions of the thoracic or lumbar cord may provoke disturbances of sensibility and vasomotor control in the upper extremities.

A CASE OF ISOLATED PARALYSIS OF THE MUSCULO-CUTANEOUS NERVE (OPERATION AND RECOVERY). OLJENICK.

This affection is distinctly rare, especially in times of peace. In the case reported there was an exostosis of the humerus which pressed on the nerve when the patient supported himself by his arms. Movements of the shoulder

were normal. The biceps was paralyzed although the supinator longus was not. The brachialis anticus was paralyzed. Anesthesia and analgesia were present along the radial border of the forearm. There was pain on pressure over the exostosis. Removal of this was followed by gradual recovery.

FREEMAN, Washington.

J. DEJERINE

1849-1917

Book Review

LE PROFESSEUR J. DEJERINE, 1849-1917. By E. GAUCKLER. Paris: Masson & Cie, 1922.

The life of Dejerine, as told in this little book, will stand as an eternal inspiration to all who love neurology, indeed to all who, devoting their lives to the effort of advancing knowledge, have the desire to push onward toward their goal in spite of hardship, in spite of disappointments, in spite of the inevitable discouragements and limitations which the enlarging horizon of increasing knowledge imposes.

Gauckler, a close friend and pupil of Dejerine, has, with delightful straightforwardness and simplicity, unfolded the story not only of the work, but also of those sides of this great Frenchman which all would have loved so much to know; the man at home, on a fishing trip, among his students and his friends, at work in his laboratory.

He takes us through school days, to Paris, through the difficult years at medical school, through his great love episode with his American wife-to-be, Miss Klumpke, his constant and devoted companion through many happy years of marriage, through intern days and laboratory work with Vulpian and through the trials of examinations for the coveted titles of "Médecin des hopitaux" and "Agregé."

His correspondence with his mother and his childhood and life-long friend, Dubois of Berne, is delightful. It shows the tenderness, the insight into life and the love of work which has made Dejerine the man so great.

Opposed by Charcot for nomination as Agregé, Dejerine proceeded to beard the lion in his den and thus gained the powerful vote of this dominating leader of the faculty. He was nominated in 1885, the order being, Brissaud, Ballet, Dejerine and Chauffard.

Two years later he began his service at Bicêtre where the tradition he founded still remains. From 1894 to 1911 he had a service at the Salpêtrière. After 1911 he became, as professor of neurology, the head of the great teaching service at that hospital, the service of the faculty. His great disappointment at not being named professor after Charcot's death left, as Gauckler has said, a certain bitterness, but his work did not suffer therefrom.

The long list of well known names of associates, friends and pupils is eloquent of the man's charm and the respect which his industry and great contributions to neurology aroused.

We go on through the three years of teaching to war days, during which Dejerine headed the military service at the Salpêtrière. He was not well in those days and no doubt did himself harm by overwork; he died during the war, in 1917.

The list of his works is astonishingly long. His great textbook, surely the best we have today, the anatomy in two volumes written in collaboration with his wife, and showing the structure of the brain as never had been done before, the volume on the spinal cord written with André-Thomas, full of invaluable material, and the work on the psychoneuroses, the interest of his last years, are in themselves enough to stamp greatness on his name. But, in

addition, nearly 300 articles appeared and on almost every important aspect of neurology. The extent of his interest was wide indeed. The greatest general contribution he made was to study series of large sections of the brain, normal and abnormal—a thing almost unknown before him and certainly not adequately used for such furtherance of our knowledge of the pathology of the brain as Dejerine made possible.

What Osler's "Aequinamitas" is to all of medicine, this book is to neurology. Gauckler has indeed done neurology a service.

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The Graduate School of Medicine, University of Pennsylvania, in cooperation with the Commonwealth Fund of New York, offers four fellowships in neuropsychiatry with special reference to child guidance. These fellowships, which are at a stipend of from $2,000 to $2,600 per annum, begin Oct. 11, 1926, and continue for a period of three years. Applications should be addressed immediately to Dr. George H. Meeker, Dean, Graduate School of Medicine, University of Pennsylvania, Philadelphia.

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